VIBRATION ANALYSIS IN THE DIAGNOSIS OF BONE MINERAL DENSITY IN HEALTHY AND OSTEOPENIC RADIUS BONE AND ITS CORRELATION TO MUSCLE STRENGTH

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RABİA HÜRREM ÖZDURAK

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Prof. Dr. Sencer Ayata
Director

I certify that this thesis satisfies all the requirements as a thesis for the degree of Master of Sciences.

Prof. Dr. Feza Korkusuz
Head of Department

This is to certify that we have read this thesis and that in our opinion it is fully adequate, in scope and quality, as a thesis for the degree of Master of Science.

Prof. Dr. Feza Korkusuz
Supervisor

Examining Committee Members

Prof. Dr. Feza Korkusuz ---

Dr. Macide Tüzün ---

Doc. Dr. Haydar Demirel ---

ABSTRACT

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Rabia Hürrem Özdurak
M.S., Department of Physical Education and Sports
Supervisor: Prof. Dr. Feza Korkusuz
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Muscle strength is assumed to be closely related with BMD, the so called determinant of bone strength, however, new methods for bone strength measurement are arising. The purpose of this study was to determine the relationship between bone mineral density (BMD), muscle strength and natural frequency of the radius in the dominant and non-dominant arm in healthy and osteopenic individuals aged between 50-70 years. Sixty sedentary male (thirty healthy and thirty osteopenic) participated this study. Bone mineral density assessment was performed by dual x-ray absorbtiometry (DEXA) and quantitative computed tomography (QCT), whereas muscle strength was measured by an isokinetic dynamometer quantitatively. Natural frequency of the radius was determined by a dual channel frequency analyzer. Differences between BMD, muscle strength and natural frequency in healthy and osteopenic participants according to dominancy were examined by Analysis of Variance (ANOVA).

Pearson Product Correlation Coefficient test was conducted to determine the magnitude of the correlation between cortical, trabecular and average BMD, muscle strength and natural frequency. Results demonstrated a statistically significant difference between BMD, natural frequency and muscle strength in the dominant arm of both groups. There was also a significant difference in the non-dominant arm in terms of BMD, natural frequency and muscle strength, except in total work in the non-dominant arms. Moreover, there was a moderate positive correlation between BMD measured by DEXA and natural frequency in the dominant arm ($r = 0,59$; $p < 0.001$) and non-dominant arm ($r = 0,64$; $p < 0.001$), whereas the muscle strength was correlated to BMD with a low positive correlation in terms of peak torque in extension ($r = ,36$; $p = ,005$), peak torque in flexion ($r = ,31$; $p = ,016$), total work in extension ($r = ,28$; $p = ,030$) and total work in flexion ($r = ,27$; $p = ,041$) in the dominant arms. The correlation between muscle strength and BMD was not significant in the non-dominant arm. The highest correlation between natural frequency and bone geometry parameters was observed in cortical thickness ($r = 0,82$; $p = 0,02$). A statistically significant positive correlation ($r = ,81$; $p = ,04$) was also observed between average BMD measured by QCT and by DEXA. In summary, according to the findings of this study, it can be concluded that vibration analysis is a precise method in predicting bone strength that depends highly on its size, shape and the distribution of its trabecular and cortical components.

Keywords: Osteopenia, DEXA, QCT, Vibration analysis, mechanical properties of radius, muscle strength, dominancy.

ÖZ

SAĞLIKLI VE OSTEOPENİK BİREYLERDE RADİUS KEMİK YOĞUNLUĞUNUN VİBRASYON ANALİZ YÖNTEMİ İLE TESPİT EDİLMESİ VE KAS GÜCÜYLE İLİŞKİSİ

Rabia Hürrem Özdurak
Yüksek Lisans, Beden Eğitimi ve Spor Bölümü
Tez Yöneticisi: Prof. Dr. Feza Korkusuz
Haziran 2004, 91 sayfa

Kemiğin dayanıklılığının belirlenmesinde önemli bir kriter olarak kabul edilen kemik yoğunluğunun, kas gücü ile ilişkisi olduğu kabul edilsede, günümüzde kemik dayanıklılığına ilişkin yeni çalışmalar yapılmaktadır. Bu çalışmanın amacı 50 ile 70 yaş arasındaki sağlıklı ve osteopenik erkek bireylerde baskın olan ve baskın olmayan kolda kemik yoğunluğu (KY), kas gücü ve radius kemiğinin doğal frekansı (DF) arasındaki ilişkiyi incelemektir. 60 sedenter (otuz sağlıklı ve otuz osteopenik) erkek bu çalışmaya gönüllü olarak katılmıştır. Kemik yoğunluğu çift enerjili x ışını abzorbsiyometresi (DEXA) ve sayısal bilgisayarlı tomografi (QCT) ile ölçülürken, kas gücü izokinetik dinamometre ile sayısal olarak tespit edilmiştir. Bunlara ek olarak radius kemiğinin doğal frekansı çift kanallı frekans ölçer ile saptanmıştır. Sağlıklı ve osteopenik bireylerin kemik yoğunluğu, kas gücü ve doğal frekansları arasında her iki kolda da fark olup olmadığı Varyans analizi (ANOVA) ile saptanmıştır.

Pearson ürün korrelasyon katsayısı yöntemi kullanılarak kortikal, trabeküler ve ortalama kemik yoğunlukları ile kas gücü ve doğal frekans arasındaki ilişkinin değeri saptanmıştır. Elde edilen sonuçlar KY, kas gücü ve DF'ın baskın olan kolda gruplar arasında istatistiksel olarak anlamlı farklılıklar gösterdiğini saptamıştır. KY, kas gücü ve DF arasındaki ilişki her iki grupta baskın olan kolda anlamlı çıkarken, baskın olmayan kolda sadece KY ve DF arasında anlamlı bir ilişkiye rastlanmıştır. DEXA ile ölçülen KY ile DF arasında ortalama pozitif bir ilşki hem baskın olan kolda ($r = 0,59$; $p < 0.001$) hem da baskın olmayan kolda ($r = 0,64$; $p < 0.001$) tespit edilmiştir. Bunun yanı sıra baskın olan kolda KY ile ekstensiyonun tepe değeri ($r = ,36$; $p = ,005$), fleksiyonun tepe değeri ($r = ,31$; $p = ,016$), ektensiyonda toplam iş gücü ($r = ,28$; $p = ,030$) ve fleksiyonda toplam iş gücü ($r = ,27$; $p = ,041$) arasında düşük ama istatistiksel olarak anlamlı pozitif bir ilişkiye rastlanmıştır. KY ile kas gücü arasındaki ilişki baskın olmayan kolda anlamsız bulunmuştur. QCT'den elde edilen kemiğin geometrik değerleri incelendiğinde, en yüksek korrelasyonun kortikal kemik kalınlığı ile DF'ın arasında olduğu gözlemlenmiştir ($r = .82$, $p = .02$). DEXA ve QCT ile ayrı ayrı ölçülen ortalama kemik yoğunluğunun arasındaki ilişkinin değeri ($r = .81$, $p = .04$) yine istatistiksel olarak anlamlı ve yüksek bulunmuştur. Özet olarak, bu çalışmanın bulgularına göre vibrasyonla analiz yönteminin, boyut şekil ve trabeküler ile kortikal kısımların dağılımına bağlı olan kemik dayanıklılığının tespit edilmesinde tutarlı sonuçlar veren bir yöntem olduğu söylenebilir.

Anahtar Kelimeler: Osteopeni, DEXA, QCT, vibrasyonla analiz yöntemi, radius kemiğinin mekanik özellikleri, kas gücü, baskınlık

To My Dad

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I hereby declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

Date: Signature:

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CHAPTER I

INTRODUCTION

Osteoporosis affects the strength and structure of bones and is a multivariable and silent disease that progresses without symptoms usually diagnosed following a fracture after a low impact trauma. Low bone mineral density (BMD) and micro architectural deterioration leading to enhanced bone fragility are determinants of this disease. Studies showed that male are equally prone to osteoporosis, although female are faced with this illness earlier because of the drastic decrease in their estrogen level during menopause. Both genders, female and male, are affected in similar proportions by fracture-related complications depending on low BMD with a higher mortality rate in males (Center et al.,1999; Diamond et al.,1997).

The consequences of osteoporotic fractures have become an increasing health problem of the world in means of life quality of individuals and health care expenses. Quality of life factors include effects on physical, mental and social health, skeletal deformity and financial resources. Activities of daily living are affected as only one-third of the patients are regained to pre- fracture level of functioning (Duncan et al., 2002; Düppe et al., 1997; Genant et al., 1999; Hyiaman et al., 1999; Jee et al., 1991; Johansen et al., 1997).

In developed countries such as USA, the expense of hip fractures reaches a value of $ 10 billion a year, whereas the cost for the incidence of hip fractures was 11.000 and for acute treatment 3 billion francs in Belgium in 1985 (Geusens et al.,

1992). The total medical costs of male osteoporosis in France amount to € 197.5 million including hospitalization, rehabilitation and convaescence in 2002 (Levy et al., 2002).

In addition to the financial burden attributed to this disease, osteoporosis has a profound effect on the quality of life of older individuals since bone mineral density (BMD) decrease with aging (Enriori and Enriori, 2002; Hasegawa et al., 2002; Johansen et al., 1997; Karlson et al., 1993) at different rates in different bones and it is difficult to completely rebuild bone that has been weakened by osteoporosis. Although hip and spine are more common areas where fractures occur as a result of osteoporosis, the life–time risk of distal forearm fractures is 15% for 50-year-old females who are around the time of menopause and 5% in men (Geusens et al., 1992). Moreover, it has been shown that risk of fracture related to secondary osteoporosis in the forearm is high among male, but not female. Osteoporosis in male remains under diagnosed, underreported, and inadequately researched (Melton et al., 2002).

Bones grow in length, width and density from birth and reach their peak BMD level between the second and third decade. Then they gradually lose density and strength with increasing age. Developing osteoporosis with increasing age depends mainly on two factors; namely (a) the peak adult bone mass and (b) the rate of bone loss which depends not only on genetic factors, age and sex hormones that can not be changed, but also on life style that can be manipulated by exercise, preventing smoking and alcohol consumption, improving nutritional condition, and by the use of certain medications (Hansen et al., 1991).

One of the alterable parameters in preventing osteoporosis is exercise. Research has demonstrated controverter results in the effect of exercise on BMD and muscle strength. Some studies have shown that exercise increases muscle strength and BMD depending on its type and duration (Landis et al., 2000; Levy et al., 2002). Swimming has low impact on BMD as gravity applied on the body in water is less than the atmosphere which in turn decreases the load on the bones. On the other

hand, weight bearing exercises such as weightlifting directly stimulates bone metabolism by remodeling under strain that results in an increase in BMD as a response to the load applied (Heinrich et al., 1990; Colleti et al., 1989; Block et al., 1986; Nilson et al., 1971)

Exercise has a wide variety of beneficial health effects; increase in muscle strength applies tension and to some extent compression on bones and increases BMD directly. Improved balance, flexibility and physical strength, which are other positive outcomes of exercise, decrease the risk of falls and subsequent fractures (Aniansson et al., 1986; Grimston et al., 1993; Kannus et al., 1995). Several studies have indicated that BMD values are highly correlated with muscle strength (Özdurak et al., 2003; Kannus et al., 1994; Kohles et al., 1996).

Effects of exercise on bone depend not only on the type, but also on the intensity and duration. Athletes who participate in gymnastics and wrestling that are sports that require muscular strength and power, result in a higher BMD than those who participate in sports depending primarily on muscular endurance (Hert et al., 1971; Lanyon, et al., 1984; Honda et al., 2001).

It has been shown that exercise has an overall effect on the whole body since there is a homeostasis in each organism and all body systems are closely related to each other (Hickson et al., 1981). On the other hand, exercising specific sites of the body may change the anatomy and physiology of that specific body part. Site-specificity of osteoporosis has been demonstrated in previous studies (Huddleston et al., 1980; Jones et al., 1977; Kannus et al., 1994). Strength of the hip muscles has been associated with forearm BMD (Snow-Harter et al., 1990). On the other hand, one study illustrated a positive relation between quadriceps muscle strength and BMD of all measured sites except the forearm (Anonymous, 1993). Some experimental studies on osteoporosis have shown that the disease may develop as a result of microgravity except that of the forearms (Landis et al., 2000; Newitt et al., 2002; Unterman, 2002; Collet et al., 1997). This may be a result of the high cortical component of the radius which is a more resistant part of the bone when compared to

the trabeculae (Landis et al., 2000). Information on the relation of forearm muscle strength and BMD is either inconsistent (Fehily et al., 1992; Francis, 2000; Frost, 2001; Jee, 1999; Jee, 2000; Jee et al., 1991; Kerr et al., 1996; Kudlacek et al., 2000) or lacking. Two studies demonstrated BMD increase in forearm bones in volleyball (Alfredson et al., 1998) and tennis players (Gradsell et al., 1989). These studies, however, did not quantitatively measure the forearm muscle strength and were interested only in BMD values of the subjects. Also several animal studies measured forearm bone breaking strength with destructive methods which is not feasible in humanbeings (Li et al., 2001; Rubin et al., 1996; Kohles et al., 1996).

Several techniques have been developed to measure forearm BMD (Newitt et al., 2002). These techniques, so far, have concentrated on the mineral content of the bone, however, their reliability greatly varied according to their application purpose (Augat, et al., 1998)

A routine x-ray can detect osteoporosis of the bone, but only when at least 30% of the bone has already been lost. In addition, x-rays are not accurate indicators of bone density, since the appearance of the bone on x-ray is often affected by variations in the degree of exposure of the x-ray film. A wide spectrum of X-ray is replaced with a narrow energy level in photon absoptiometry, but still influenced by fat when it's single photon absorptiometry (SPA). Dual-energy X-ray absorptiometry (DEXA) with little radiation exposure is currently used as a standard in the diagnosis of osteoporosis and monitoring, preventing and/or treating the disease, since photons with different energy levels have different attenuation coefficients while crossing different tissues. Substances emit X-rays in two different ways, scattering and true absorption which together create the total absorption measured by the quantity "absorption coefficient". DEXA gives an average BMD in terms of g/cm^2 including cortical and trabecular components of the bone (Pearson, 1992). These BMD values are biased with bone size and cortical thickness (Carter et al., 1992), and with soft tissue (Bolotin et al., 2003). DEXA measures only mineral density and gives almost no information on the organic part (collagen) of bone that is as important as its mineral component when mechanical strength is considered. Furthermore, the long

and short term precision error of DEXA instruments is higher than expected. (Korkusuz et al., 2004).

Quantitative Computed Tomography (QCT) is a highly sensitive BMD scan used in the diagnosis and follow-up of osteoporosis. Measurements related to components of the bone such as trabecular width, cortical thickness, geometry, BMC, BMD, apparent density may be obtained by QCT, and is not affected by structural deformities and implants that increase the BMD result in DEXA. Although it is one of the most reliable and precise technique for the measurement of BMD available today, its precision and accuracy depends highly on the observer and skilled performers are needed. In addition to its relatively high radiation dose when compared with DEXA, the differences in definitions of BMC and BMD, sensitivity of results, difficulties in subject positioning, consistent slice location, requirement of daily calibration and its expense make the use of QCT technically difficult (Dequeker et al., 1993).

It is assumed that osteoporosis can be detected non-invasively with different methods that can also monitor response to therapy or geometry of bone which give new insights to bone metabolism in humans (Newitt et al., 2002; Matsumoto et al., 1994; Yang et al., 1994). Not only the peripheral, central and entire skeleton, but also components such as trabecular and cortical regions of a single bone can be studied by novel methods. However these techniques vary in degree of accuracy, precision and discrimination and differ substantially in fundamental methodology, clinical and research utility, and general availability (Carter et al., 1992), and with soft tissue as well (Bolotin et al., 2003; Korkusuz et al., 2004). Therefore, further investigations should be carried on to find new methods in osteoporosis diagnose which may overcome these limitations.

Vibration analysis in particular is becoming increasingly popular as a predictive maintenance procedure and as a support for machinery maintenance decisions since it is possible to determine both the nature and severity of the defect, and hence predict the machine's failure. (Nicole et al., 2003). Moreover, it is widely

used to determine characteristics of isotrophic and anisotrophic layers (Nayfeh et al., 1991),and random elastic media (Karaesmen et al., 1976). Not only engineering, but also medical sciences use wave propagation techniques in identifying some disorders (Abu-Alshaikh et al., 2001).

It seems reasonable that wave propagation technique, so called vibration analysis may be applied as a new technique in diagnosis of not only decreased BMD and collagen, but also geometrical changes in bone without any radiation exposure. This technique may overcome limitations of DEXA and QCT which can be applied in certain intervals because of high radiation dose. Vibration analyses will also fit with the requirements of the sports area since this technique may be field applicable with its appropriate instrumentation and low cost.

1.1 Hypothesis

It is assumed that (1) vibration transmission will provide adequate information on bone strength in superficial bones of the human body such as the radius.(1.a) There will be at least a moderate positive correlation between vibration transmission and BMD measured by QCT and DEXA. (1.b) Trabecular, cortical and average BMD measured by QCT will affect the magnitude of correlation of natural frequency. Furthermore, (2) there will be a relation between forearm muscle strength and BMD.

1.2 Purpose of the Thesis

Since osteoporosis is an increasing health problem all over the world with high socio-economic consequences and a high impact on individuals life quality, the effect of exercise in preventing osteoporosis turns to be an important aspect. Little is known on the relation between muscle strength and the forearm BMD in males. Osteopenic bone differ not only in BMD value from osteoporotic one, but also in geometry caused by different modeling and remodeling mechanisms according to the

Utah paradigm (Frost, 2001) supported by experimental studies (Newitt et al., 2002; Rubin et al., 1996). From this point of view, using only BMD values obtained mostly by DEXA should be questioned. In the present study BMD was measured quantitatively by DEXA. Results of DEXA were compared to a field applicable and mechanical method called vibration transmission, since it is hypothized that bones that loose their density in osteoporosis will effect the natural frequency also expressed as the resonance of the bone, related to architectural deterioration and increased porosity. QCT images of both healthy and osteopenic individuals were obtained and correlated to BMD and natural frequency values to understand the change and behavior of the bone during osteoporosis in cortical and trabecular components. All BMD values obtained by DEXA and QCT and natural frequency were correlated to muscle strength which was also measured quantitatively by an isometric dynamometer. The dominant and non-dominant arms were assessed and compared in both groups.

1.3 Dependent and Independent Variables

Subjects were classified according to the independent variable health status as (a) healthy individuals with a radial T score higher than -1, and (b) osteopenic individuals with a radial T score between -1 and -2.5. Subgroups were established according to dominancy as (a) dominant forearm and (b) non-dominant forearm. The dependent variables in the first part of this study with 60 subjects including 30 healthy and 30 osteopenic individuals were BMD, natural frequency and muscle strength measured as peak torque in extension and flexion, and total work in extension and flexion. The dependent variables in the second part of the study based on QCT measurements of seven subjects were total, trabecular and cortical BMD and geometrical properties of measured as bone diameters in x and y axis, trabecular width in x and y axis, and cortical thickness in radius, and natural frequency in both dominant and non-dominant arms.

1.4 Expectations

1. Differences between groups and subgroups

1.1 Healthy subjects will have higher BMD, muscle strength, natural frequency and QCT values related to a higher mechanical strength in the forearm compared to osteopenic individuals.

1.2. There will be a difference in vibration transmission in the forearm between groups and subgroups.

2. Correlation of bone geometry parameters, natural frequency and BMD values

2.1. There will be a relation in cortical and trabecular bone thickness and width and density in both groups and subgroups.

2.2. There will be a correlation between BMD and vibration transmission values in both groups and subgroups.

2.3. There will be a correlation between BMD, natural frequency and QCT measured in seven subjects.

2.4. There will be a correlation between BMD and muscle strength in all groups

1.5 Limitations

The study was limited to 60 male participants; 30 healthy and 30 osteopenic. Osteoporotic individuals were not included. Osteopenic group was defined according to distal radial BMD measured by DEXA. Osteopenic individuals were under medication for their disease. The age range was 50-70 years. Only seven subjects were involved in QCT measurements. Eating and exercise habits of participants was not questioned.

CHAPTER II

THE SKELETAL SYSTEM

2.1 Anatomical Terminology

Anatomical position, which refers to a person standing erect with arms hanging to the sides and with the head, feet and palms of the hand directed forward, is the reference point for comparisons to promote clarity in understanding in human parts and motion (Gray,1966; Seeley, Stephens and Tate,1999).

Proximal refers to the part of the limb that is nearest to the point of attachment, whereas distal is just the opposite. Anatomically, the distal portion of a limb or other part of the body is that portion that is most remote from the point of reference. Median and lateral are terms used to describe surface relationships with respect to the median line of the body, which is an imaginary line on a plane dividing the body into right and left. The term medial is applied to the surface of structures that are closest to the median line, whereas lateral refers to the farthest part with respect to the median line.

There are imaginary planes that section the body into different parts and give us the opportunity to observe body structures from inside. The medial plane, also referred as the midsagittal plane, runs vertically through the trunk and divides the body into left and right parts. Any plane parallel to the medial plane is termed the sagittel plane. Planes passing through or running parallel to the coronal suture in the

skull and divide the body into anterior and posterior halves by intersecting the medial plane vertically are termed frontal or coronal planes. The planes that runs parallel to the ground and are drawn at right angles to the medial and the frontal planes divide the body into superior and inferior parts, are termed as horizontal or transverse planes(Leeson and Leeson, 1972;).

2.2 Human Skeleton

The skeletal system forms a solid framework around which the body is constructed. It consists of bones, cartilage and ligaments. This system provides support and protection for the softer parts of the body. Delicate organs such as the lungs, brain, heart and spinal cord are protected by the bony enclosure which is hold together by ligaments and constituents the skeletal system. In addition to protection, the bones provide points of attachment for muscles, which act as levers when the muscle contract in order to make movement possible. Furthermore, skeletal system is also responsible for mineral storage and blood cell production. The mineral component of the bones provides a pool of calcium, phosphorus and other ions that may be utilized to stabilize the mineral content of the blood and whole body. Both red and white blood cells are formed in the marrow of certain bones of the body with respect to blood cell genesis.(Seeley, Stephens and Tate,1999)

The human skeleton is composed of 206 bones differing in each individual and age since bones may fuse together with increasing age. It has two main parts called axial skeleton and appendicular skeleton which are further divided to subparts. The axial skeleton is the part of the skeleton which consists of the skull, the vertebral column and the thoracic cavity, whereas the appendicular part is divided into upper and lower extremities. Each upper extremity consists of a pectoral girdle, arm and hand. The pectoral girdle consists of a scapula and clavicle where the upper part of the arm, called humerus, is attached. The lower arm consists of two bones; one is the radius which is lateral to the other one called ulna. The lower extremities consists of the pelvic girdle, formed by ossa coxae and symhysis pubis, and the legs consisting

of the femur in the upper leg and tibia parallel to fibula in the lower leg attached to the upper leg with patella.(Gray,1966;Seeley, Stephens and Tate,1999).

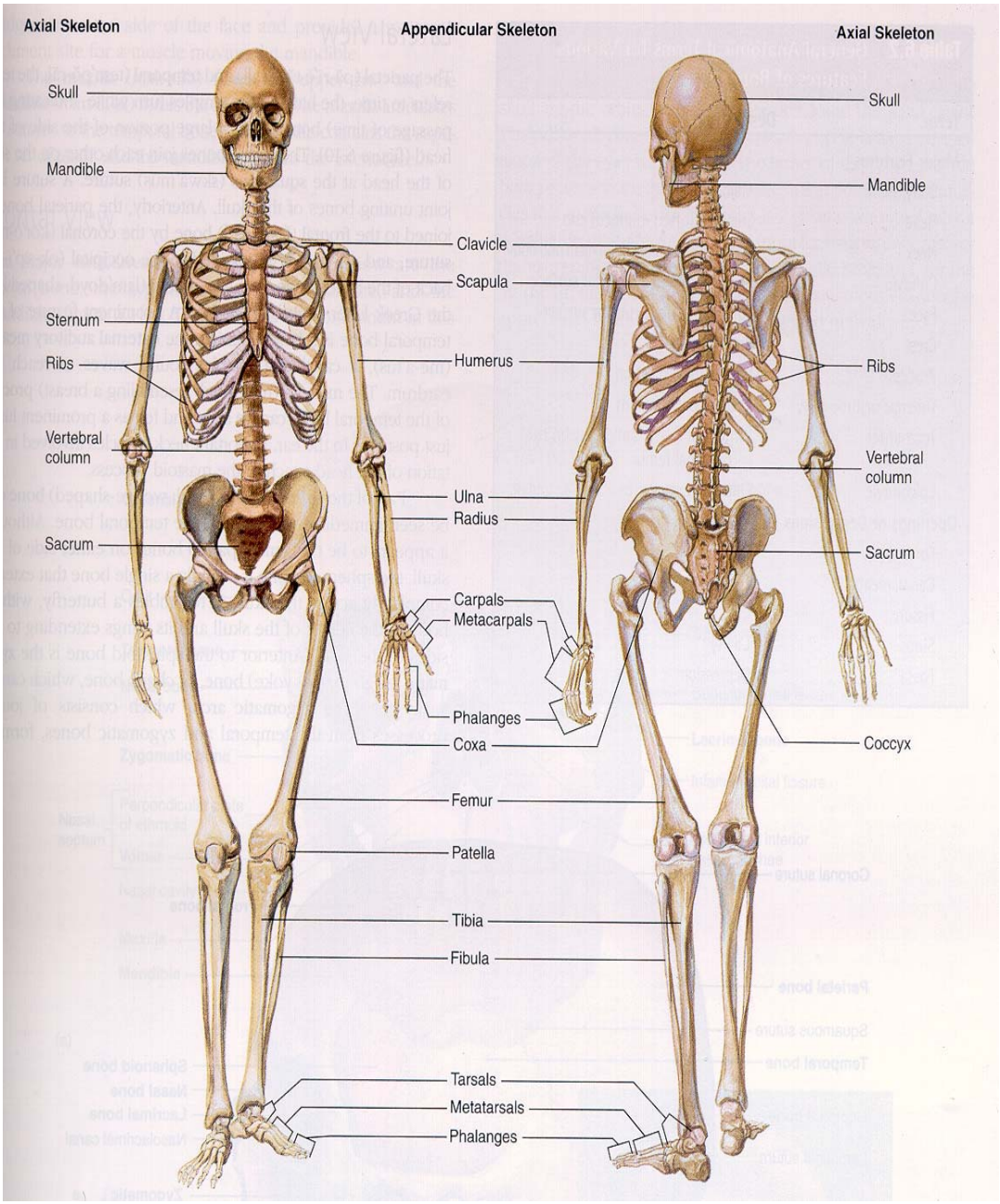

Figure-2.1 Bones of the skeletal system in anterior and posterior position(Seeley, Stephens, and Tate; 1999)

2.3 Types of Bones

The bones in the skeleton are grouped according to their appearance and differ in their composition. They are classified as long, short, flat and irregular bones. The long bones include the bones of the arm such as radius and leg such as tibiae with a complex structure made up of many different tissues. Long bones will be described in details in section 1.4. Short bones, seen in the wrist and ankle, are not only equal in their principal dimensions, but also differ from the long bones in respect that they are filled with cancellous bone instead of having a medullary cavity. The protective bones of the skull, the ribs, sternum and the scapulae are called flat bones which consists of cancellous bone and marrow surrounded by two layers of compact bone. Irregular bones, composed of cancellous bone and marrow enveloped within a thin layer of compact bone and irregular in their shape, are located in the vertebrae and middle ear. Round bones embedded in tendons, such as the patella in the quadriceps femoris tendon, are called sesamoid. Sesamoid bones consist of cancellous bone and marrow enclosed in compact bone. Long bones include the bones of the arm, leg, metacarpals, metatarsals and phalanges which are tubular in shape and its length dominates its width.(Lockhart et al,1972; Seeley, Stephens and Tate,1999)

2.4 Structure of the Long Bones

Each long bone is composed of a central shaft namely diaphysis, with epiphysis on both ends covered with articular cartillage for articulation. Epiphyses are classified as pressure epiphyses, occurring in the line of weight transmisson, traction epiphyses, occurring at attachment sites of certain muscles as a result of muscular pulling, and atavistic epiphyses which were independent bones ones, but fused with other bones. The epiphyseal plate or growth plate which is responsible for growth of the bone is located between these two structures and is named as an epiphyseal line when it becomes inactive after the bone has reached a certain maturation and stops growing.(Muschler et al., 2001)

Long bones are made up of a large medullar cavity in the diaphysis and smaller cavities in the epiphyses filled with red marrow, responsible for blood cell formation, and yellow marrow consisting mostly of fat. The red marrow, which is located in flat and short bones, the articular ends of the long bones, sternum, ribs and bodies of vertebrae, dominates the yellow marrow in the childhood, however, it is replaced by yellow marrow with increasing age.

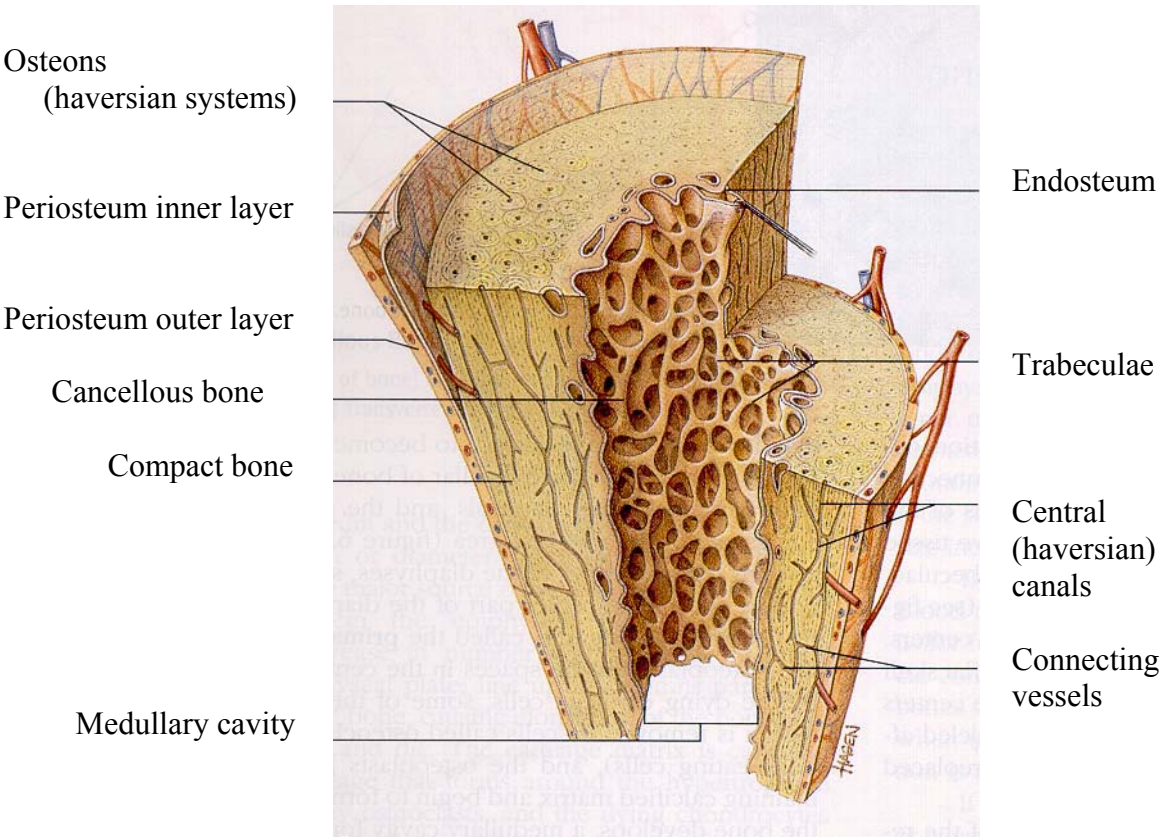

Figure-2.2 Internal features of a part of a long bone (Seeley, Stephens, and Tate; 1999)

The nourishment of the bone is obtained via the blood vessels and stimulation occurs via the nerves which are both connected to the periosteum which is a though and dense connective tissue that envelops the surface of the entire bone except for the areas of articulation which are covered with smooth articular cartilage that is of the hyaline types. The absence of functional periosteum causes either decreased or no osteogenic potency and does not contribute to the healing of fractures. A thinner connective tissue membrane, the endosteum, is aligned on the surface of the

medullary cavity and possesses osteogenic properties, too (Bloom and Fawcett, 1968).

2.5 Bone Tissue

Tissue that makes up the bones of the skeleton meets all criteria of connective tissue, however, it has many unique features. It is hard, strong and relatively light weighing and can be visualized as living organic cement. It arises from cartilage and fibrous connective tissue precursors during fetal development. Collagenous fibers serve as a framework for gradual deposition of calcium and phosphate salts by osteoblasts which are responsible for bone growth, repair and remodeling.(Seeley, Stephens and Tate,1999)

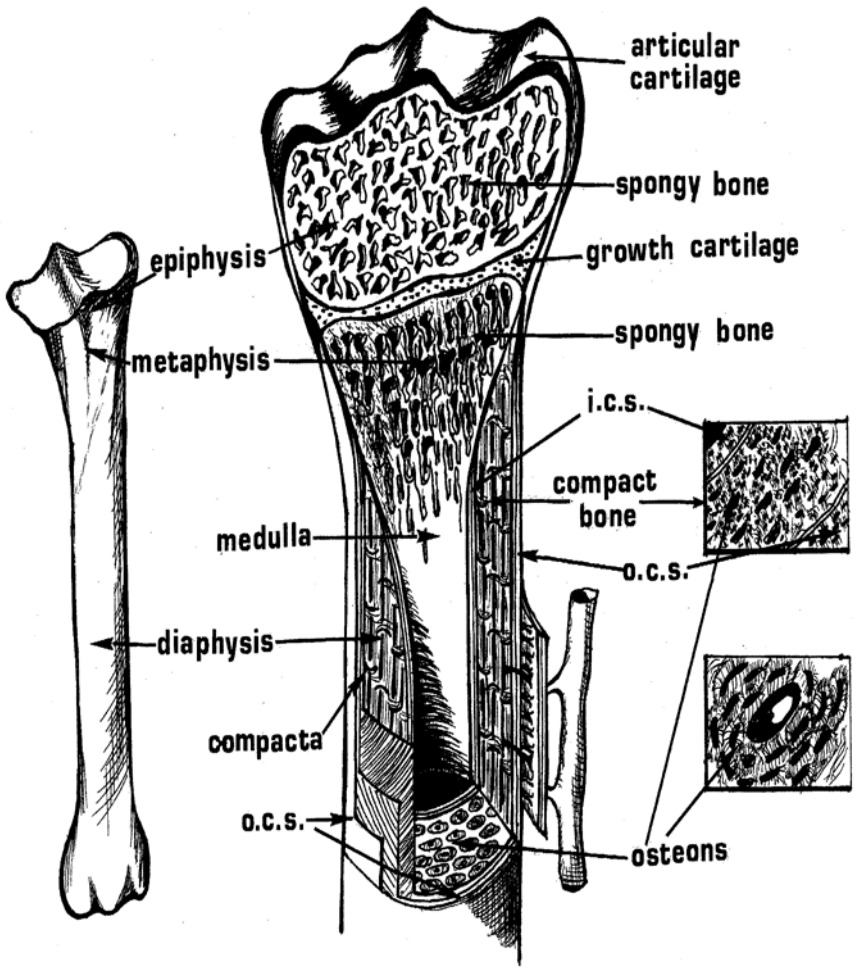

Figure-2.3 Components of a young long bone (Hall, 1991)

In macroscopic level, there are two frameworks apparent which are called compact bone and spongy bone. The compact bone which makes up the outermost layer is solid and dense, whereas the spongy bone, also called cancellous bone, has a porous structure with different histological characteristics.

Compact bone is permeated by a framework of tunnels, channels and interconnecting networks that are surrounded by a hard matrix. The functional and structural part of the compact bone is the osteon which has a cylindrical shape and the harvesian canal containing one or two blood capillaries located in the hollow found in the center. Surrounding each central canal are several concentric rings of matrix called the lamellae. Osteocytes, responsible for matrix secretion, are located within small hollow cavities, called lacunae, which are oriented between the lamellae with several hollow tunnels, called canaliculi, radiating outward, imparting a spider-like appearance. Intimate contact between the protoplasmic processes of adjacent osteocytes through the canaliculi makes it possible to recieve nourishment and exchange materials within the hard space of matrix of the entrapped osteocytes (Seeley, Stephens and Tate,1999).

The spongy bone lies adjacent to compact bone and continuous without a distinct line of demarcation. From the histological point of view, it's organization is in a lesser degree than the cancellous bone. It is composed of a series of branching,

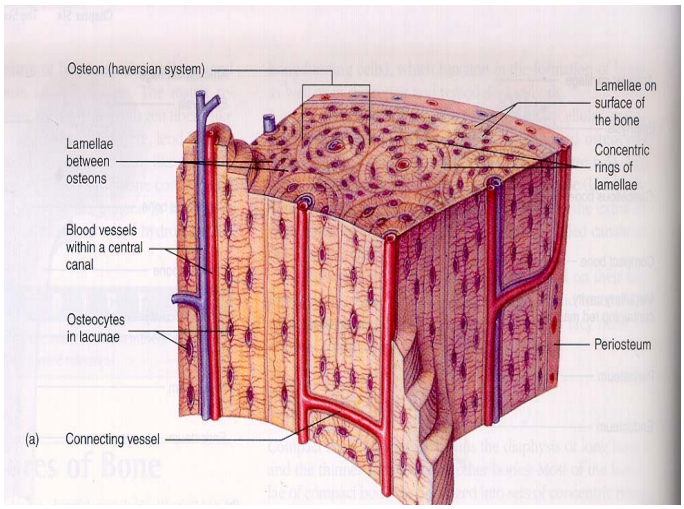

Figure-2.4 Fine structure of a compact bone (Seeley, Stephens, and Tate; 1999)

overlapping plates of matrix called trabeculae that are oriented in all planes so that they make up large, interconnecting cave-like spaces, serving as pockets for holding blood-forming cells and storage, thereby reducing weight.

According to the functional requirements of the bone, these two tissue types differ in their quantity in each bone and different parts of the same bone. To withstand bending stresses, cortical bone quantity dominates the trabecular bone quantity in the middle of the shaft of long bones (Bloom and Fawcett, 1968).

2.6 Mechanical Properties of Bone Tissue

The anisotrophy, lack of linearity, elastic properties and heterogeneous structure of the bone make the mechanical analyses very complex and difficult. The adaptation mechanism of the bone to metabolic and environmental changes in vivo triggers this complexity in understanding the mechanical properties. Many variables that characterize the bone have been identified so far in order to understand the relation between the structure and mechanical behavior of the bone (Han et al.,1995).

2.6.1 Definitions related to mechanical properties

Static and dynamics are the components of mechanics. Static studies bodies at rest or in an equilibrium state where sum of forces and moments equal zero, whereas dynamic studies are described either as kinematics which is the geometry of motion such as relation among displacement, velocity and acceleration, or as kinetics that deals with the effect of force on the geometry of motion.

Force (F) or load which are the measures that have a magnitude, direction and point of application, tend to change the velocity of the body as an external effect or the shape of the body as an internal effect. The change in shape, structure and morphology in bones result from the force effects. Forces are classified as compressive, tensile and shearing according to their direction with different effects on the bone.

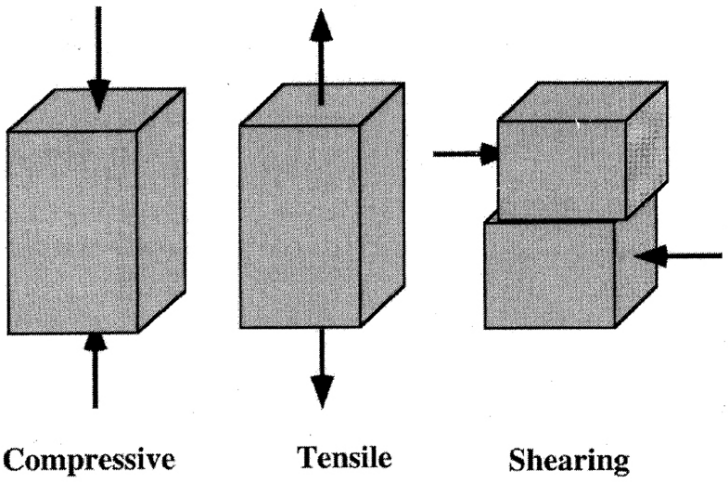

Figure-2.5 Types of forces (Hall, 1991)

Stress which is defined as the internal resistant of a material, arises from the forces between molecules, collagen fibers and hyroxyapatite crystal bonding in bones. Since it is the ratio of F divided by area, they are classified as compressive, tensile or shear according to the direction and characteristic of the force.

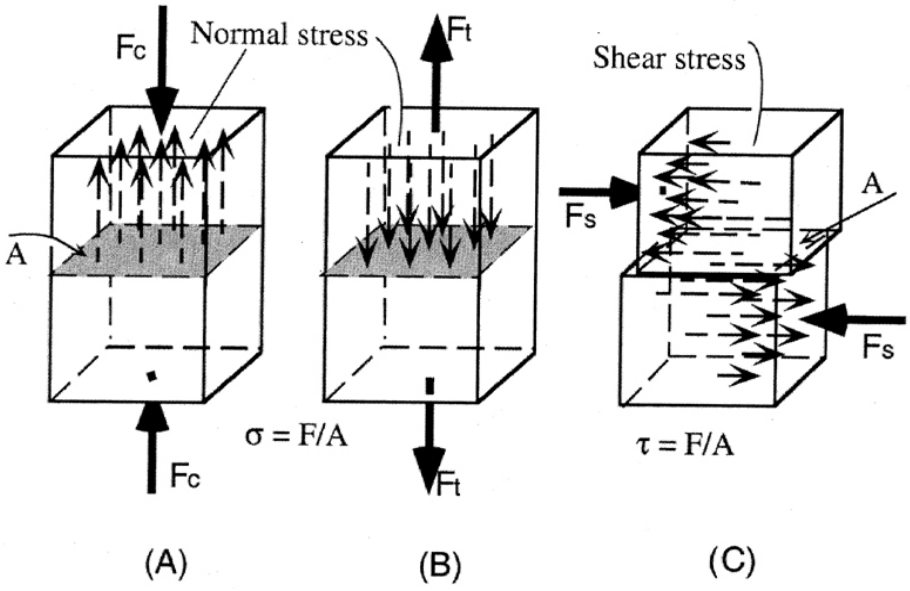

Figure-2.6 Stresses of a bone as a response to applied forces (Hall, 1991)

Strain, on the other hand, is defined as the geometric change of the substance under the action of force. This dimensionless measure can be expressed as deformation in the bone. The stress-strain plot gives the ability to calculate the elastic modulus of the substance by measuring the slope of the curve in elastic region. The

area under the stress-strain curve shows the energy absorbed of an object under loaded conditions. Loading a bone cyclically with progressively higher forces produce a highly nonlinear stress-strain curve. This produces micro damage that increases with each load cycle and results in intensity variance during testing.

Strength is defined as the internal resistance of a material to deformation and fracture. Yield strength is defined as the stress that causes a specific amount of deformation, whereas ultimate strength is the stress required to fracture the bone. Toughness, termed as work of fracture, is the energy required per unit volume of a material to perform fracture. Repetitive stress under the ultimate stress value applied on bone may cause the fatigue. Moreover, fatigue fracture in bone results from the stresses imposed on skeleton by musculature during movement. Endurance fatigue limit, on the other hand, is the maximum stress to which a bone can tolerate without any deformation. Elasticity, on the other hand, is the ability of a substance to return to its original shape after the removal of the stress. If the stain is dependent on time, it will be termed as viscoelasticity. The creep and stress relaxation properties of viscoelastic materials such as bones, are mainly used to quantify mechanical properties of bone. Stress relaxation is the decay of stress within a material under constant strain, whereas creep is the gradual increase in strain of a material under constant load.

2.6.2 Mechanical properties of the bone

Bone is an elastic, nonlinear, viscoelastic, anisotrophic, heterogeneous and composite material. It is determined according to its mechanical properties such as density, porosity, microscopic structure such as trabecular volume, cortical thickness and architecture, etc. However, the cortical and trabecular sides show different mechanical characters and should be handled separately. The dense nature of cortical bone determines its strong and stiff mechanical properties compared to trabecular bone.

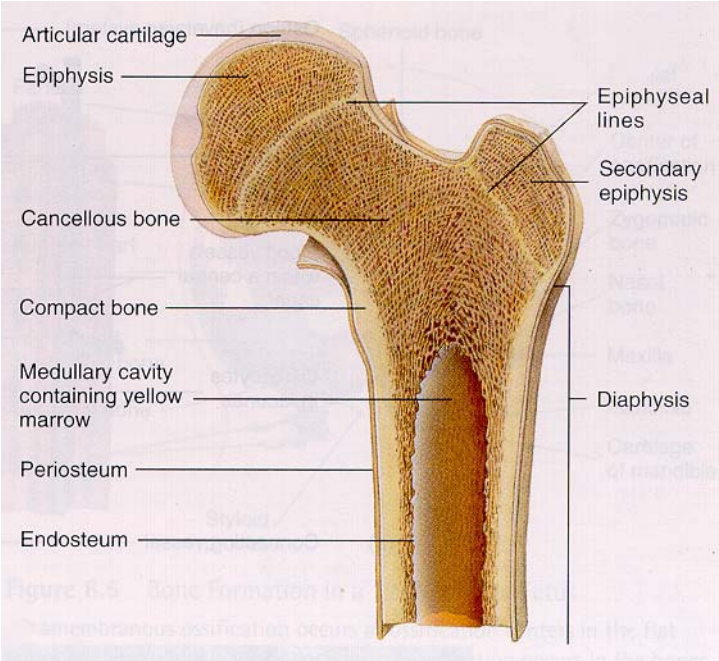

Figure-2.7 Frontal section with differing cortical and trabecular components through the end of an aduldt long bone (Seeley, Stephens, and Tate; 1999)

Depending on the type of testing, the elastic modulus and strength of the cortical bone range from 14.7 to 34.3 Gpa and from 133 to 295 Mpa, respectively. The bending mechanical properties of a long bone are determined by its tubular shape and bone densities, while that of a cortical bone is determined by osteonal direction. The apparent and material densities are mostly equal in cortical bone since it does not contain space. It is nearly equal to 1.9 g/cm^3 (Katz et al., 1989).

BMD and BMC are positively correlated with strength and stiffness of bones such as ulna. Porosity, which is defined as the ratio of void volume to total volume, is less than resulting in an increased mechanical strength when compared to trabecular bone (Jurist et al., 1977).

The elastic modulus of trabecular bone is less than cortical bone (Rho et al., 1993). Moreover, analysis of strength and stiffness of both cortical and trabecular bones stated that the bone can be modeled as a continuum (Martin et al., 1992).

2.7 Bone Cells

Although bone cells are classified under three categories, they transform from one type to another. Therefore, it can be thought that osteoblasts, osteocytes are different functional states of the same cell type, whereas osteoclasts originate from haemopietic cells (Hall, 1991). Moreover, tissue engineering studies showed that different types of cells may develop into bone cells under appropriate stimulation (Stein et al., 1993).

Osteoblasts, which contain endoplasmic reticulum, golgi complex and mitochondria, synthesize the collagen fibrils that form the bulk of organic matrix.

This structure serves as a scaffold upon which Ca5(PO4)3OH mineral phase is located. When the mineralization of the bone matrix reaches a certain level, osteoblasts transform into osteocytes by reducing their cytoplasmic content and decreasing their endoplasmic reticulumn and golgi amount. Although they loose their matrix forming property, they gain their communication ability to maintain homeostasis through their intersitial substance and fine-connecting cytoplasmic channels build up by osteoblasts.

Figure-2.8 Electron photomicrograph of osteoblast forming bone. Dark material at bottom is mineralized bone. The lighter, interposed material is osteoid (Hall, 1991).

Moreover, they have an active role in transportation of substances between blood and bone. Not only osteoblasts, but also osteocytes have the ability to be tranformed into osteoblasts when they are released from their lacunae.

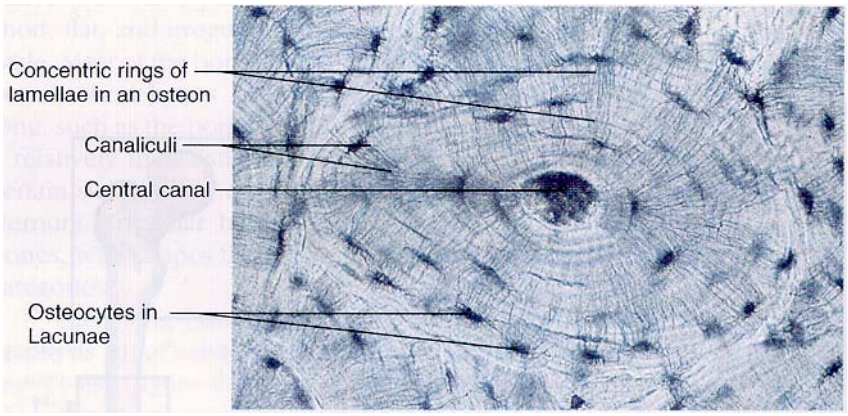

Figure-2.9 Photomicrograph of compact bone (Seeley, Stephens, and Tate, P.; 1999)

Osteoclasts, located on the periphery of the trabeculae, are mainly responsible for the removal of calcified cartillage matrix by forming long villous processes on their bone facing surface when the growing trabeculae reaches a certain thickness. Since they are responsible for bone resorption, they contain lysosomes in addition to polyribosome, endoplasmic reticulum cisternae and many smooth vesicles in different size. Bone resoption occurs through the formation of a sealing zone of adhesion between the osteoclasts and the bone extending around the circumference of the bond-apposed surface of the osteoclast (Miller et al., 1984).

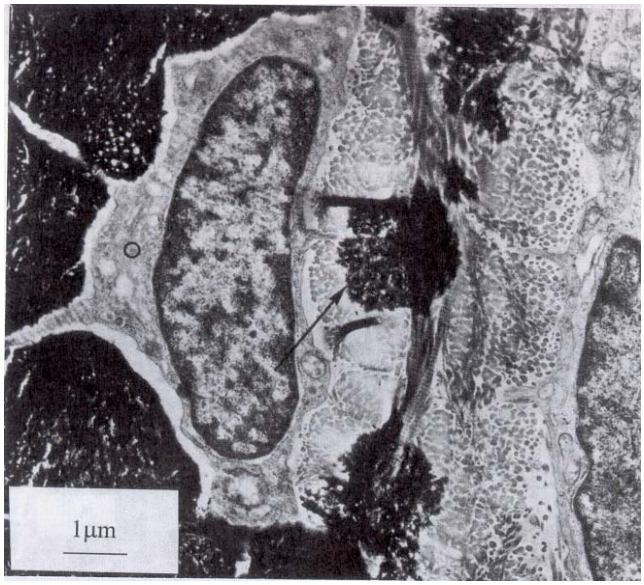

Figure-2.10 Electron photomicrograph of osteoclastic activity (Hall, 1991)

2.8 Bone Metabolism and Homeostasis

All bones develop by increasing their width and length until adolescence. As stated earlier, the increase in the length of a bone occurs in the epiphyseal plate by the means of increasing the numbers of chondrocytes within the proliferating zone and line up parallel to the long axis causing elongation.

Intramembranous ossification is the term used for production of bone in connective tissue membranes by osteoblasts such as in the skull. The osteoblasts start to deposit bone matrix in order to form the trabeculae in the ossification centers which radiates as a little network of spicules consisting of osteogenic fibers. These fibers give rise to fresh bone spicules by a continuous ossification and growth to the peripheral part of the related bone. The ossification centers yield as the fusion areas of two flat bones and thickening of the trabeculae ends up with its remodeling and is replaced with compact bone.

Figure-2.11 Electron photomicrograph of ossification (Hall, 1991)

The ossification from cartillage with a general shape of the mature bone is termed as endochondral ossification. Fibroblasts of the perichondrium, which covers the cartillage, start to enlarge and become bone forming osteoblasts around the center of diaphysis. The perichondrium is named as periosteum after it starts to form bone. The place in the center of the diaphysis, where bone cells first start to appear are called the primary ossification center. While some of the cartillage cells are dying and some of the calcified matrix is removed by the osteoclasts, osteoblasts fill up the remaining calcified matrix and start the formation of lamelae. This phenomenon is called the “creeping substitution”. Secondary ossification centers form also in the epiphyes after the replacement of calcified matrix with medullar cavity filled with bone marrow by the action of osteoclasts has been finished. The newly formed spongy bone is transformed into compact bone by bone destruction and resorption and ossification is completed when epiphyses fuse to diaphyses and growth in length is no longer possible for the bone.

The replacement of existing bone with newly formed osteoblasts is termed as remodeling, which give rise to growth and changes in shape of the bone when it is located in the epiphyses. While growth in length and width occurs via the deposition of new cells on the outer surface of the bone, some bone is removed from the inner medullar cavity resulting in a constant compact bone thickness. The effect of calcium in remodeling process will be discussed in Chapter III.

When bones of the body are subjected to excessive stress, fractures are likely to occur which cause blood vessel damage. The bleeding vessels give rise to clot formation on the damaged site which is invaded by surrounding tissue. The gap between the broken parts in the fracture is filled with not only fibrous network produced by these cells, but also islets of cartillage are produced. The area, where tissue repair occurs is termed as callus. Osteoblasts starts to form cancellous bone in the callus, and immobilization is a must at this time period, since refracturing of the sensitive and fragile newly formed matrix may occur as a result of movement. At least, cancellous bone will be remodeled to compact bone as described previously with a complete healing period of several months.

2.9 Mineralization of Bone

Bones, which are continuously remodeled, are the body's main calcium reservoir, since 99% of the calcium is deposited within the bones. The homeostasis of calcium in an organism is under hormonal control. The hormones responsible for calcium metabolism are parathyroid hormone(PTH), an 84-residue polypeptide responsible for the increase in calcium concentration in serum via resoption from bone and kidney and increase in the dietary calcium absorption in the intestine, vitamin D, a steroid-like substance working synergistically with PTH, and calcitonin which in a 33-residue polypeptide functioning in the inhibition of calcium resorption from bone and kidney and giving rise to a decrease in serum calcium level. PTH does not only inhibit osteoblast activity and stimulate osteoclast activity, but also increase the rate of phosphate excretion from the kidney, which results in calcium leaching out of bones in order to increase serum calcium concentration. PTH's other function is the activation of vitamin D, which enhances the transfer of intestinal calcium to the blood. Improper mineralization or calcium metabolism will cause abnormalities in muscle contraction, nerve impulse transmission, blood clotting, hormonal signaling and bone structure (Voet and Voet, 1995).

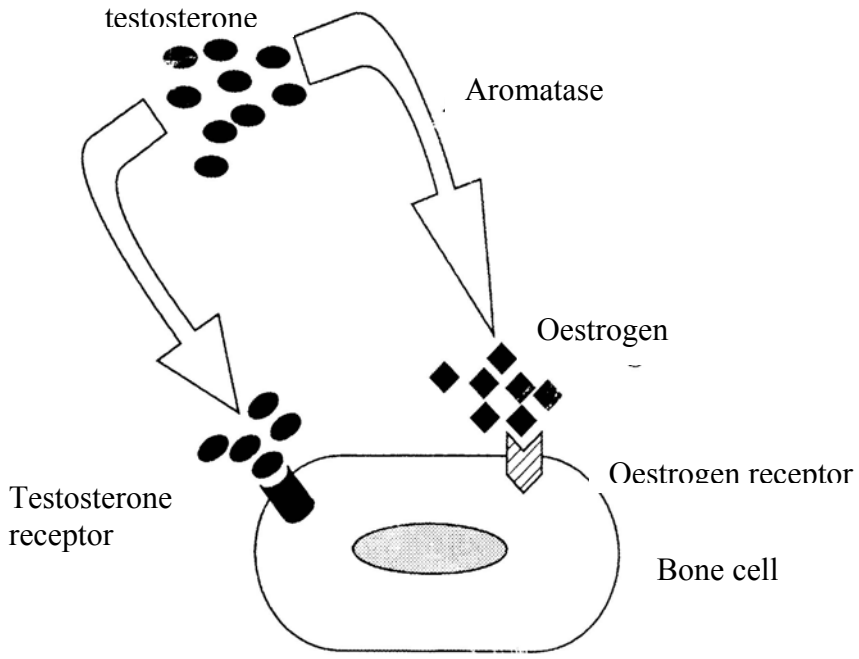

Figure-2.12 Mechanism of the effect of sex hormones on remodeling.

CHAPTER III

EFFECTS OF EXERCISE ON BONE

3.1 Attachment site of bones for muscles

Bones are irregularly-shaped structures with depressions called fossa, lumps called tubercle, and projections called process which serve as muscle attachment sites. Each muscle of the body is said to have an origin and insertion. The origin of the muscle is the immovable end, whereas the insertion is the other end which moves during contraction that results in the shortening of the distance between the two ends.

Muscles may be attached to bones in three different ways; directly to the periosteum, by means of a tendon, and with an aponeurosis. Tendons are white fibrous tissues with different lengths that provide a connection of muscle to the skeleton.

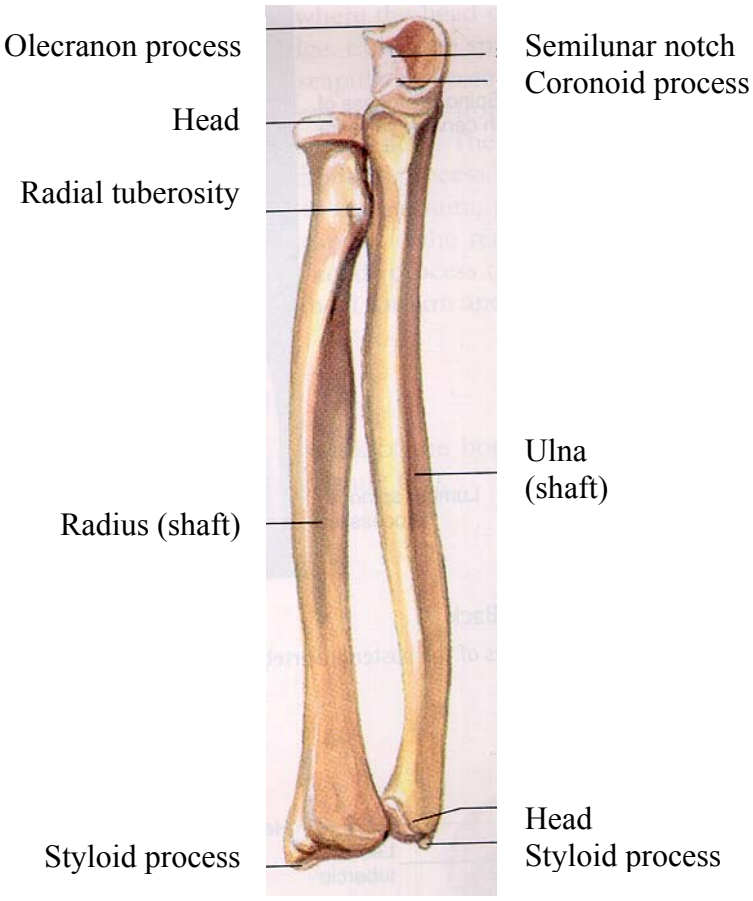

Figure-3.1 Anterior view of right ulna and radius (Seeley, Stephens, and Tate; 1999).

3.2 Types of movements

The action of muscles through diarthoric joints results in a variety of movement types. The nature of movement is dependent on the construction of the individual joint and the position of the muscle. When the angle between two parts of a limb is decreased, this movement is termed as flexion. On the other hand, when the angle between two portions of limb or two parts of the body increases, this is called extension. The movements of a limb away from or toward to the median line are termed as abduction and adduction, respectively. The movement of a bone arround its longitudinal axis without lateral displacement is named as rotation. When the rotational movement of a limb occurs through a freely movable joint and draws a circle, it is termed circumduction. The movements such as raising the palm from

downward to upward, are called suppination, whereas the opposite movement is called pronation (Seeley, Stephens, and Tate; 1999).

Muscles may work either alone or together. The flexors are the prime movers, or agonists, whereas opposing muscles contribute to smooth movements by their power to maintain tone and give way to movement by the flexor group. Variance in the tension of flexor muscles results in a reverse reaction in the extensor muscle. Muscles that assist the agonists to reduce undesired action or unnecessary movement are called synergists, and muscle groups that hold structure in position for action are called fixation muscles.

3.3 Forearm muscles

3.3.1 Muscles responsible for forearm movements

The principal movers of the forearm are the biceps branchii, branchialis, branchioradialis and triceps branchi. Biceps branchii is the largest muscle on the anterior surface of the upper arm that bulges when the forearm is flexed. Its origin consists of two tendinous heads: a medial tendon attached to the coracoid process, and a lateral tendon that fits into the intertubercular groove on the humerus. The latter tendon is attached to the supraglenoid tubercle of the scapulae. These two heads form a single insertion on the opposite end which binds to the radial tuberosity of the radius and are responsible for flexion of the forearm, outward movement of radius in addition to hand suppination.

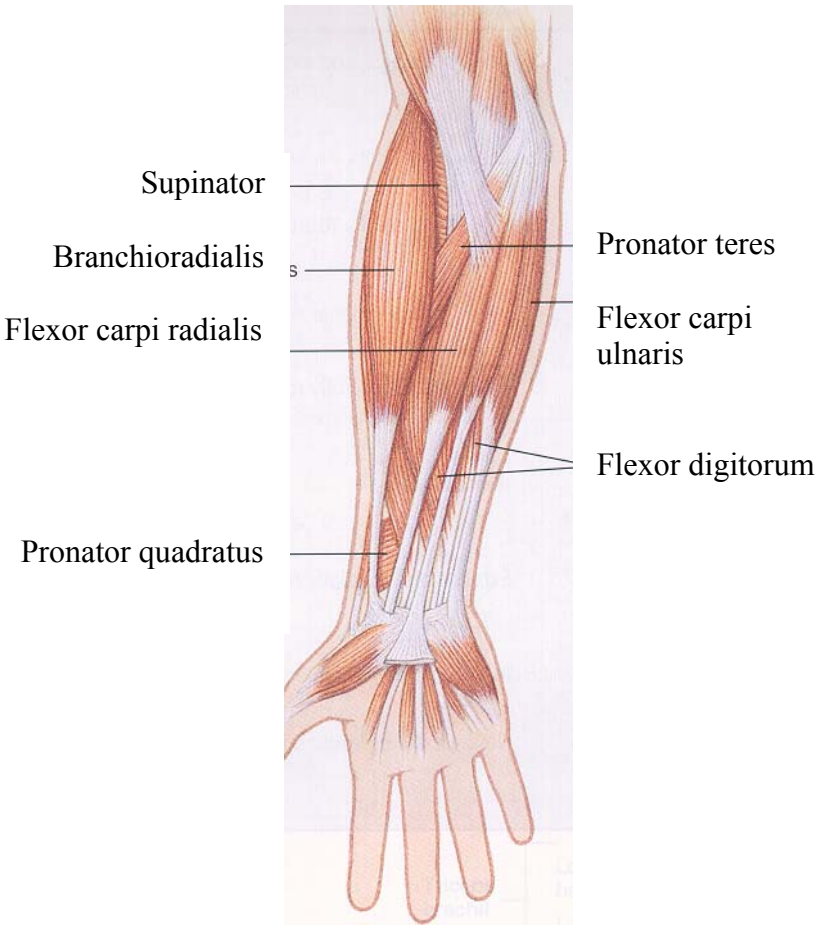

Figure-3.2 Anterior view of the muscles of the forearm (Seeley, Stephens, and Tate; 1999).

Branchialis which is located immediately under the biceps branchii on the distal anterior portion of the humerus, orginates on the lower part of humerus. Its insertion is attached to the front surface of the coronoid process of the ulna giving rise to forearm flexion.

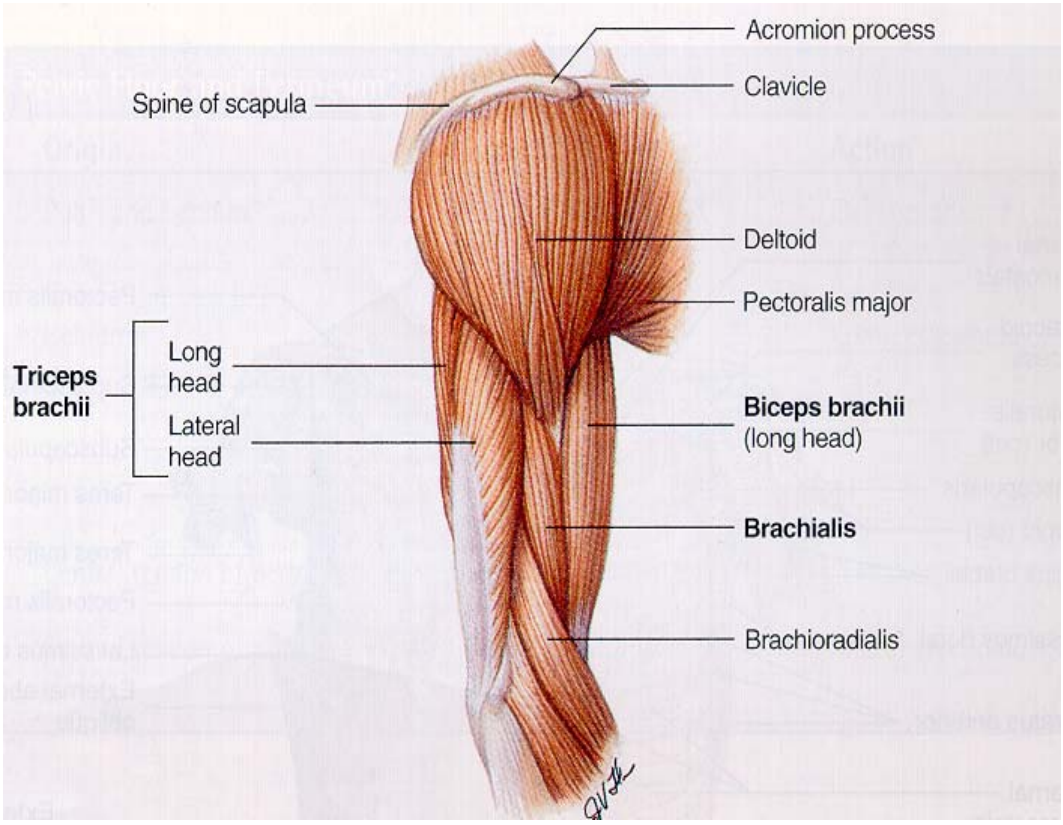

Figure-3.3 Muscles of the anterior shoulder and arm (Seeley, Stephens, and Tate; 1999).

Branchioradialis, is the most superficial muscle on the lateral, or radial, side of the forearm orginating above the lateral epicondyle of the humerus and inserting on the lateral surface of the radius slightly above the styloid process, acts in forearm flexion.

The entire back surface of the brachium is covered by triceps branchii with three heads of origin; a long head arises from the scapulae, a lateral head from the posterior surface of the humerus, and a medial head from the surface below the radial groove. The tendinous insertion of the muscle is attached to the olecranon process of the ulna and it is not only responsible for forearm extension, but also works as an antagonist of the branchialis.

3.3.2 Muscles responsible for hand movements

Supination and pronation of the hand are carried out with muscles that originate or insert on either radius or ulna. The supinator is a short muscle near the elbow that arises from the lateral epicondyle of the humerus and the ridge of ulna. It curves around the upper portion of the radius and inserts on the lateral edge of the radial tuberosity and the oblique line of the radius. Pronation is achieved by the pronator teres which originates on the medial epicondyle of the humerus and inserts on the upper lateral surface of the radius.

Pronator quadratus originates on the distal portion of ulna and inserts on the lateral portion of the radius with the same function; proniation. Flexor carpi radialis arises on the medial epicondyle of the humerus and inserts on the proximal portion of the second and third metacarpals. Another flexor of the hand is the flexor carpi ulnaris, originating from the medial epicondyle of the humerus and posterior surface of ulna. Its insertion consists of a tendon that attaches to the base of the fifth metacarpal. While both muscles flex the hand, the radial muscle causes abduction and the ulnaris muscle causes adduction of the hand.

The flexor digitorum superficialis flexes all fingers, except the thumb. It arises on the humerus, ulna and radius. Its insertion consists of a tendon that is attached to the middle phalanges of the second, third, fourth and fifth fingers.
The flexor digitorum profundus lays directly under the flexor digitorum superficialis and originates on the ulna and the interosseous membrane between the radius and ulna. It inserts with four tendons on the distal phalanges of the second, third, fourth and fifth fingers. This muscle flexes the distal portion of the fingers. The flexor pollicis longus arises on the radius, ulna and interosseous membrane between these two bones. Its insertion consists of a tendon that is anchored to the distal phalanx of the thumb. It flexes only the thumb.

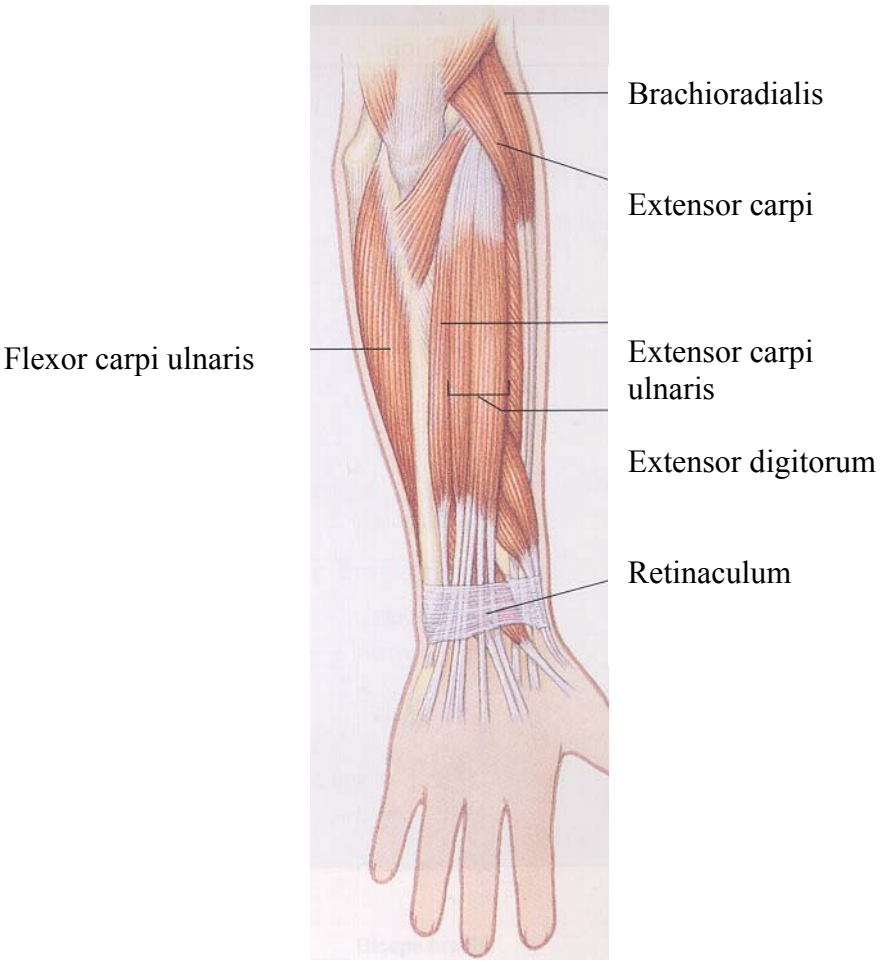

Figure-3.4 Posterior view of the muscles of the forearm (Seeley, Stephens, and Tate; 1999).

The extensor carpi radialis brevis is medial to the the extensor carpi radialis longus. Both muscles originate from the humerus, with the longus taking a more proximal position. The longus inserts on the second metacarpal; the brevis on the middle metacarpal. The extensor carpi ulnaris is the third muscle involved in extending the hand. It arises on the lateral epicondyle of the humerus and part of the ulna. It inserts on the fifth metacarpal. The extensor digitorum communis that lies alongside the extensor carpi ulnaris, arises from the lateral epicondyle of the humerus and inserts on the distal phalanges of fingers two through five. It extends all fingers except the thumb. The extensor pollicis longus, extensor pollicis brevis, and abductor pollicis move the thumb. The longus muscle arises on both ulna and radius. It inserts on the distal phalanx of the thumb. The brevis muscle, which lies superior to longus, inserts on the proximal phalanx of the thumb and assists the longus in extending the

thumb. The abductor pollicis originates on the interosseous membrane and inserts on the lateral portion of the first metacarpal and trapezium. Its action is only the abduction of the thumb as easily guessed from its name.

3.4 Effect of exercise on musculoskeletal system

3.4.1 Mechanical Control of Bone Modeling and Remodeling

Healthy load bearing bones respond to continuous low, normal and heavy loads by modeling and remodeling (Frost, 1997a). Bones are strained and deformed by static and dynamic mechanical loads and slowly start to increase their strength to reduce later strains around the threshold range. Static strains do not cause adaptive responses whereas dynamic strains which change at high physiological rates such as high-impact loading, engender adaptive responses (O'Connor et al., 1982; Lanyon et al., 1984). These adaptive responses are modeling which occurs only when mechanical load applies strain on bones that exceed the modeling threshold that is genetically-determined as the "Minimum Effective Strain" range for mechanically controlled bone modeling. Bone (re)modeling occurs according to the highest strain applied so that they become strong enough to keep typical peak strains which may exceed the threshold and can cause injuries in future. This actually makes bones stronger than needed for their voluntary loads and is termed as the strength-safety factor. This factor is expressed as the ultimate strength divided by the modeling threshold when both are considered in stresses, where the ultimate strength refers to the maximal load a bone can carry. Therefore, exercise plays an important role in modeling, since bones adapt their strength to past and present voluntary physical activities. Physical activities can be described as low-impact such as swimming, normal impact such as normal such as walking, and high-impact such as weight-lifting and gymnastic (Burr,1998; Burr et al., 1995; Forwood and Turner, 1995; Frost, 1990 a,b; Jee and Frost 1992; Martin et al., 1998; Martin, 2000; Umemura et al., 1997).

An experimental study with adult rat showed that modest overloading of one of the hind-limbs gave rise to increased expansion of the subperiosteal bone area and reduced expansion of the marrow cavity in the related bone. This resulted in an increase in both cortical bone and percent cortical bone mass thereby increased diapyhseal structural rigidity when compared with immobilized contra-lateral hind-limbs which were the controls. Furthermore, bone resorption was inhibited, although endocortical labeling was surprisingly unchanged. It was concluded that overloading inhibited bone marrow and increased periosteal expansion with tendency to increase net formation drift in modeling direction by depressed bone remodeling (Jee et al., 1991).

3.4.2 Effect of type and intensity of exercise on bone mineral density

Regular exercise depending on its type and intensity change bone strength by increasing BMD during growth and helps to maintain it throughout the life. Exercise has been shown to have a beneficial effect on the growing skeleton by acting to maximize peak bone mass which is determined 60% genetically (Young et al., 1995; Adami, 1994). Physical training can also prevent or reverse the involution loss of bone with age (Forwood and Burr, 1993). The exercise program in order to increase bone mineral density should be based on weight-bearing activity which means exercise beyond normal activities of daily life that require loading principles (Frost, 2001).

In a previous study, hundred-twenty-four postmenopausal women with decreased BMD aged between 50 and 70 performed one hour weight-bearing exercise three times a week for one year. No further decrease in BMD was observed, whereas BMD decreased significantly in the non-exercising control group. Moreover, the exercising group showed reduced back pain with increased fitness and well-being which prevented falling related fractures as a result of increased balance and flexibility (Bravo et al., 1996). Although cross-sectional human studies showed that weight lifters have higher BMD than endurance athletes (Granhed et al., 1987; Heinrich et al., 1990; Heinonen et al., 1993), few studies reported a trend towards greater BMD

in young and middle-aged women after strength training (Snow-Harter et al., 1992; Huddleston et al., 1980).

Not only the type, but also the intensity of exercise plays a determinant role in the effect of exercise on BMD. A seven month lasting study with 33 postmenopausal women showed that performing brisk walking above the anaerobic threshold for half an hour three times per week may increase BMD up to 1.1% while the control groups who walked under the threshold or did not walk at all lost 1.0% and 1.7% BMD, respectively (Hatori et al., 1993).

Duration of the activity is another parameter of exercise and critical in BMD. A comparative population based study showed fracture prevalence differences between individuals in cities and in rural areas who are exposed to heavier workload as a result of longer duration (Jonsson et al., 1993).

Another population based study of 332 randomly selected subjects aged between 15 and 42 years supports these findings in addition to show the radius as an exceptional region of the skeleton based on the response to physical activity. That study found a statistically significant positive correlation between quadriceps muscle strength and BMD at all sites measured in adolescent men, except the radius (Düppe et al., 1996). Increase in the radius with high cortical bone has been observed by direct loading of forearm as stated in the studies with tennis players and rowers (Wolman et al., 1990; Jones et al., 1977; Pirnay et al., 1987). These studies suggest that the effect of loading on bone is site-specific and BMD increases may be observed primarily in the loaded part of skeleton. The long term unilateral activity of regular tennis playing was associated with increased BMD in the playing arm compared with the contra lateral arm of the same individual thereby reducing the effects of confounding factors such as age, gender, height, weight, nutrition, and genetic influence. The site-specific BMD increase in the side-to-side comparison was highest in the humerus and least in the ulna (Kannus et al., 1994).

Based on the studies above, it can be concluded that exercise depending on its type, intensity and duration may affect BMD and bone strength in a site-specific manner, however, this effect diminishes short after termination of exercise since loads applied on bones disappear which turns the modeling off. A study showed an increase in BMD of postmenopausal women who walked or jogged in addition to weight-bearing exercise three times per week for an hour for one year. 15 of these subjects stopped weight-bearing after one year that resulted in a loss of BMD whereas the rest of the subjects who followed the whole exercise program retained their gained BMD values (Dalsky et al., 1988). Moreover, exercising in a gravity reduced environment such as swimming may cause decreased bone mineral density in the whole skeleton with more severity in the trabecular bone (Heinrich et al., 1990). This decrease resembled the microgravity dependent bone loss seen in animals and astronauts (Landis et al., 2000; Newitt et al., 2002; Unterman, 2002; Collet et al., 1997). Also heavy training may have an adverse effect on BMD. It may cause reduced bone growth and induced BMD loss with site specific cancellous bone adaptation and decreased osteoblastic activity rather than a global adaptation of bone remodeling (Bourrin et al., 1994).

CHAPTER IV

OSTEOPOROSIS

4.1 Definition of Osteoporosis

The term Osteoporosis is derived from French, osteoporose, to describe the porosity of the bone in 1824. Sir Astley Cooper had described the condition of low bone mass as "thin in their shell and spongy in their texture" and prone to fracture after minimum trauma (Consensus Development Conference, 1991).

Osteoporosis is clinically defined as "a disease characterized by low bone mass and a micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk" (World Health Organization, 1994).

Osteopenia and osteoporosis are accepted to be the degrees of the same bone illness. The numerical expression of osteoporosis measured by DEXA may be interpreted as either Z or T scores. These terms are referred as the number of standard deviations that the individual's BMD is away from the age-matched mean and young adult normal mean, respectively. Osteopenia is defined as a T score between -1 and -2.5, while osteoporosis is defined as a T score at or below -2.5. Severe or established osteoporosis includes the presence of a fragility fracture (WHO, 1994).

Osteoporosis is a major public health threat. The World Health Organization has defined osteoporosis as a priority health issue affecting more than 150 million people worldwide and filling more hospital beds than any other disease. Overall, one in three women and one in eight men aged over 50 will have an osteoporosis-related fracture in their lifetime (Elffors et al., 1994).

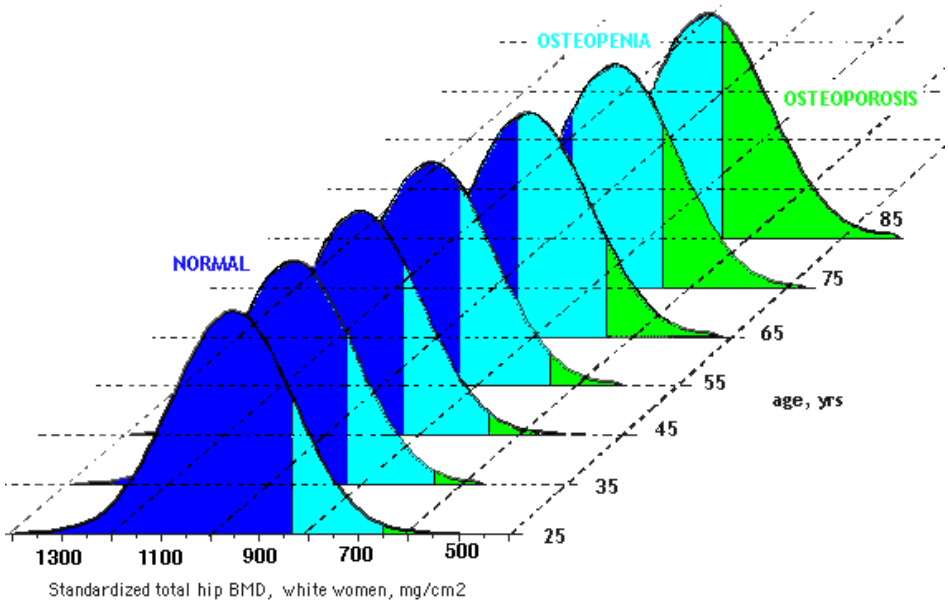

Figure-4.1 BMD values classified as healthy, osteopenic and osteoporotic (WHO).

Worldwide, the lifetime risk for a woman to have an osteoporotic fracture is 30-40%. The most commonly observed osteoporotic fractures affect the vertebral body, distal radius, and proximal femur. In men the risk is about 13% (Cummings et al., 1995).

4.2 Classification and Causes of Osteoporosis

Since osteoporosis is a multivariate systematic bone disease, it is classified according to its physiopathology and cause. The most common types of osteoporosis are sensile osteoporosis and postmenopausal osteoporosis which reflect gender-specific bone mineral density reductions (Genant et al., 1985).

Postmenopausal Osteoporosis is characterized by excessive and disproportionate trabecular bone loss, rather than cortical bone, and is hormonal in origin. The decrease in bone mineral density in the lumbar spine can be approximately 50 % from ages 20 to 80 years (Mosekilde et al., 1987).

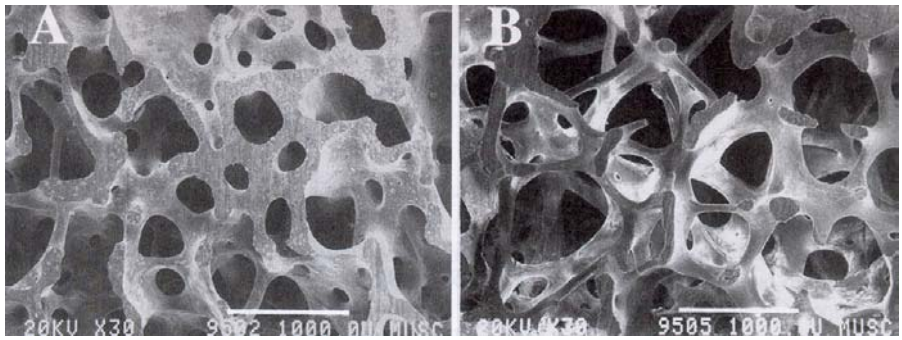

Figure-4.2 Photomicrograph of the trabecular bone in (a) healthy and (b) osteoporotic bone (Hall, 1991).

Post-menopausal osteoporosis is the direct removal of bone tissue dependent on imbalanced anabolic and catabolic steroid interactions. After the menopause, women's oestrogen levels fall and as oestrogen is responsible for regulating bone growth and absorption this has an immediate effect upon bone density. This type of osteoporpsis may be seen not only in women 5 to 10 years after menopause, but also in individuals of any age who take steroids for therapeutic purposes (Bockman and Weinerman, 1990).

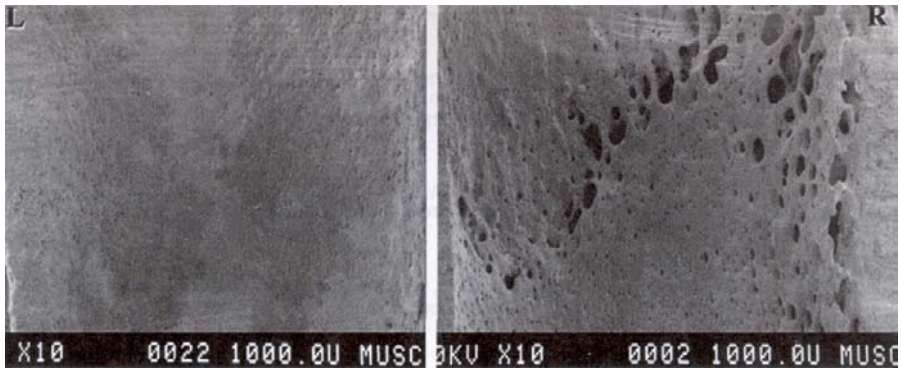

Figure-4.3 Photomicrograph of the cortical bone in (a) healthy and (b) osteoporotic bone (Hall, 1991).

Both males and females over 70's suffer from senile osteoporosis where breakdown and bone reformation is being disturbed. Sensile osteoporosis is characterized as loss of both cortical and trabecular bone mass in differing degrees by natural ageing process (Wang et al., 2001).

Modulus and strength properties of cortical bone deteriorate progressively with aging same for men and women (Burstein et al., 1976; Currey, 1969).

Moreover, aging result in a decrease in BMD number and thickness in the trabeculae, whereas the size and intertrabecular space increase (Bergoth et al., 1988; Aaron et al., 1987; Mosekilde and Mosekilde, 1990). Vertical loss of trabecula may alter structural integrity in a damaging manner because new bones can be formed only on existing surfaces (Parfitt et al., 1983).

The reduction in density, decrease in thickness and increase in length, also termed as triple jeopardy, contribute to the weakening mechanism of the trabeculae. A study demonstrated that uniaxial compressive strength of trabecular bone may be reduced by an order of magnitude by 10 over 6 cycles of loading (Michel et al., 1991). The fatigue failure in trabeculae is higher than the cortical bone giving rise to buckling of individuals trabeculae often seen among old people (Snyder and Hayes, 1990).

Remodeling occurs by basic multicellular units (BMU). Bone turn over occurs in small packets by resorbtion of some bone via osteoclasts activity and filling the hole with new bone by osteoblast activity (Jee, 1989). This remodeling is conservative, completed BMU's resorb and produce nearly equal amount of bone, therefore no significant gain or loss in the bone mass has been observed until the fifth decade in life. However, if this remodeling occurs in a disuse mode because of strains lower the threshold that is needed for remodeling, BMU's absorb more bone tissue than they produce, which result in a decrease in both trabecular and endocortical bone next to or close to marrow (Frost, 1998). Decrease in bone mineral density of astronauts (Unterman, 2002; Colletti et al., 1997) and human subjects up

to 40% aged between 30 and 75 years (Marcus et al, 1996) may be explained with the disuse-mode remodeling. The disuse-pattern osteoporosis is characterized as decreased spongiosa, thinner cortex and enlarged marrow cavity with no change in diameter of the bone.

4.3 Physiopathology of Osteoporosis and the effect of exercise

Bone was thought to be a static tissue in earlier concept, but this has changed gradually. Bone tissue undergoes various dynamic changes including appositional growth, resorption and modeling. Even gross aspects of bone may vary with age. Total amount of bone in the skeleton is controlled by the remodeling cycle and decreases in different degrees in different bone components with increasing age . Trabecular bone mass peaks in the second decade, whereas cortical bone mass peaks in the first half of third decade which undergo remodeling 40 % and 10 %, respectively every year in a health individual.(Hayward and Caggiano, 1987).

Bone turnover is regulated not only by systemic hormones such as oestrogens by their inhibitory effect on osteoclast activity, but also by local factors (Spelsberg et al., 1999).

The normal adaptive response of bone cells which accurately matches bone structure prevailing weight bearing, changes dramatically with the depletion of oestrogens giving rise to decreased osteoblast activity and increased osteolclasts apoptosis resulting in a loss of bone (Dempster and Lindsway, 1993).

Since oestrogen promote tubular reabsorption of calcium, it is not surprising that urinary calcium excretion rises during menopause and triggers the bone loss (Nordin et al., 1991).

Moreover, it is known that physical activity increases BMD which seems to be mediated by the release of insuline-like growth factors by osteoblasts which promote the proliferation of these cells under mechanical stimuli (Minaire, 1989).

It is well known that both low calcium intake and immobilization have adverse effect on BMD loss separately; however, there are also some studies that have examined their combined effect on BMD (Lau et al., 1992; Mazess and Barden, 1991). An experimental study with ovariectomized rats has shown that the combined effect of exercise and calcium intake is more beneficial in preventing BMD loss than only calcium supplementation itself. They concluded that calcium supplementation does not produce any significant increase BMD. These results agree with the hypothesis that exercise produces a positive effect in BMD both directly and indirectly because exercise decreases bone resorption and increases bone formation (Gala et al., 2001).

4.4 Factors effecting Osteoporosis in males

Primary and idiopathic osteoporosis with no risk factors accounts for 40 % in males, whereas hypogonadism, steroid therapy and alcohol consumption cause 40-50 % secondary type osteoporosis (Francis, 2000; Bilezikian, 1999). Steroid treatment to cure rheumatoid arthritis and obstructive pulmonary disease result in decreased testosterone levels which cause osteoporosis. Decreased osteocalcin levels also have been observed in corticosteroid-treated patients (Eastell et al., 1998). Hypogonodal osteoporosis is associated with low Vit D levels, malabsoption of calcium and reduced oesradiol levels, and accounts for 20 % for the factors causing osteoporosis among male. It effects cortical bone development before puberty. Renal failure is another factor of osteoporosis since it increases mineral loss deposited in the bones (Eastell et al., 1998).

Osteoporosis results not only as a result of excess bone loss without adequate replacement, but also may develop due to bone loss alone if a person never reached peak bone mineral density during childhood and adolescence. Peak bone mineral density in male is determined 60 % by genetic factor, however, adequate androgen levels and normal timing of puberty play also important roles in peak bone mineral density which is achieved by the age 18 years. Bone growth is also influenced by

dietary calcium intake and exercise not only during childhood, but also adolescence (Bilezikian, 1999; Eastell et al., 1998).

Two studies showed that testesterone derived oestrogen, especially its receptor pathway, in male has vital importance in attainment of peak bone mineral density. A mutation in the aromatase gene resulted in elevated testosterone level and decreased oestradiol level since aromatase enzyme plays role in conversion of testosterone to oestradiol. Bone mineral density increased as a response of estrogen therapy with restoration of hormone level (Morishima et al., 1995; Carani et al., 1997).

The second study showed that no change occurs in testosterone levels whereas oestradiol levels elevate several times higher than normal in a mutation in oestrogen receptor gene. This resulted in severe osteoporosis which was resistant to estrogen therapy (Smith et al., 1994).

Sedentary life style in addition to tobacco and alcohol consumption is important in bone loss among males (Hoidrup et al., 1999; Hoidrup et al., 2000). Even free radicals have been shown to be involved in bone resorption stated by a negatively associated correlation between 8-iso-PGF2α that is a major F2-isoprostane and a biomarker of oxidative stress (Voet and Voet, 1995) and BMD (Basu et al., 2001).

CHAPTER V

VIBRATION ANALYSIS

5.1 Techniques used in determination of bone parameters

There are several techniques which can use the bone parameters that are the point of interest in osteoporosis. Biomechanical testing helps to understand the mechanical properties of the bone by using engineering tools. Two groups of biomechanical tests can be applied; (a) destructive tests which are not feasible in human studies since at the end of testing the shape or some properties will have changed, and (b) nondestructive tests where specimens keep their original shape and properties.

Several noninvasive tests which can measure bone components such as cortical and trabecular bone at axial and appendicular parts of the skeleton with different degrees of accuracy and precision have been developed in order to detect osteoporosis and monitor the degree of response to the therapy. The most common methods are radiographic absorptiometry (RA), single X-ray absorptiometry (SXA), single-photon absorptiometry (SPA), dual X-ray absorptiometry (DEXA), dual-photon absorptiometry (DPA), quantitative computed tomography (QCT), peripheral quantitative computed tomography (pQCT), quantitative magnetic resonance (QMR), magnetic resonance microscopy (μMR), and ultrasound technique (Newitt et al., 2002).

All these techniques differ in accuracy, precision and discrimination. Moreover, they differ in their cost and clinical and research utility. RA measurements precision errors have been published varying from 0.3 to 4.8% and this method is limited to phalanges and metacarpals which are least effected parts in osteoporosis. (Matsumoto et al., 1994; Yang et al., 1994). A routine x-ray can detect osteoporosis of the bone, but only when at least 30% of the bone has already been lost. In addition, x-rays are not accurate indicators of bone density, since the appearance of the bone on x-ray is often affected by variations in the degree of exposure of the x-ray film and a wide spectrum of X-ray which is replaced with a narrow energy level in photon absoptiometry, but still influenced by fat when its single photon absoptiometry (SPA). Dual-energy X-ray absorbtiometry (DEXA) with little radiation exposure is currently used as a standard in the diagnosis of osteoporosis and monitoring, preventing and/or treating the disease, since photons with different energy levels have different attenuation coefficients while crossing different materials. Substances emit X-rays in two different ways, scattering and true absoption which together create the total absoption measured by the quantity "absoption coefficient". DEXA gives an average BMD in terms of g/cm^2cm including cortical and trabecular components of the bone (Pearson, 1992). These BMD values are biased with bone size and cortical thickness (Carter et al., 1992) and with soft tissue as well (Bolotin et al., 2003). DEXA measures only mineral density and gives almost no information on the organic part (collagen) of the bone that is as important as its mineral component when mechanical strength is questioned. Furthermore, the long and short term precision error of DEXA instruments is higher than expected. (Korkusuz et al.; 2004).

Quantitative Computed Tomography (QCT) is a highly sensitive BMD scan used in the diagnosis and follow-up of osteoporosis. Measurements related to components of the bone such as trabecular width, cortical thickness, geometry, BMC, BMD, apparent density may be obtained by QCT, and is not affected by bone conditions, such as structural deformities, metal objects, including hip replacements and spinal rods, that increase the BMD result in DEXA. Although it is one of the most reliable, precise techniques for the measurement of BMD available today, its

precision and accuracy depends highly on the observer and skilled performers are needed. In addition to its relatively high radiation dose when compared with DEXA, the differences in definitions of BMC and BMD, sensitivity of results, difficulties in subject positioning, consistent slice location, requirement of daily calibration and its expense make the use of QCT technique difficult. pQCT parallels QCT in many aspects with an additional limitation such that it is applicable to the peripheral skeleton (Dequeker et al., 1993).

Recently, QMR and μMR have been developed for diagnosis based on detectable MR signals in magnetic fields. These are actually a limitation of QMR, since compact bone does not generate any detectable MR signal like soft tissues or gross skeletal structure. The improved QMR is still limited to the trabecular part of the bone with a precision error of 3.8 – 9.5% and does not give any idea about the cortical region which plays an important role in , especially secondary osteoporosis (Grampp et al., 1995). Moreover, the precision of the appearance of image in MR depends on several factors other than the image resolution such as pulse sequence that can be spin-echo or gradient-echo, the echo time, and the magnetic strength. The more precise method based on magnetic resonance imaging is μMR microscopy, however, the need for taking biopsy samples is its biggest limitation since it is a painful process and therefore, can not be applied periodically (Majumdar et al., 1995).

There are tests to measure BMD and bone strength which can be categorized as static tests or dynamic tests. Static tests require displacement of the bone of interest, and measure only the strength of bone, whereas dynamic tests also predict BMD and are noninvasive. Dynamic tests can be subdivided into sonic and ultrasound tests. Quantitative Ultrasound Testing becomes a popular technique since it is low in cost, does not exposure radiation, however, their precision errors are high because of soft tissue effects on results(Faulkner et al., 1994).

Another method similar to the principles of ultrasound is vibration analysis involves the mechanical excitation of an object and the analysis of the recorded

subsequent response. Dynamic forces are applied by hammer impact and the response can be analyzed in terms of vibrations and wave propagation (Van der Pere Belgium).

5.2 Vibration Analysis

In theory, it is possible to monitor various pathological and trauma-induced conditions ranging from fractures through to osteoporosis and artificial hip joint loosening by applying a stimulus to bone and analyzing the response (Nokes, 1999). Mechanical impedance measurements can be performed by measuring the force of the impact and the peak heights of the decaying response measured by an instrumented hammer and accelerometer (Streitman et al., 1979).

5.3 Basics of Sonic Methods

The wave can have many shapes, but fundamental to each is a wave length and a natural frequency. The wave length is the distance along the x axis after which the shape of the wave begins to repeat itself. The natural frequency of the wave is the frequency at which any string element repeats its transverse oscillations due to the passage of the wave.

$$f_n = \frac{1}{2\pi}\sqrt{\frac{k}{m}}$$

f_n: natural frequency (Hz)

k: spring stiffness

m: mass

When this dynamic equilibrium between stiffness and inertial (mass) force is disturbed by damping, the resonant frequency shifts to a lower frequency called natural damped frequency f_d;

$$f_d = f_n\sqrt{1-\xi^2}$$

ξ is the damping ratio

Damping to some extend is present in each real structure and cause loss of energy resulting in the decay of movement. The same formula can be applied to the bone where K is the generalized stiffness representing the structures elastic resistance to a deformation , and M is the generalized mass representing the structures inertial resistance to accelerations inherent to the movement. As seen from the formula; the square of natural frequency is proportional to the stiffness, bone, and inversely proportional to mass. Generalized stiffness is replaced as bending stiffness which is Young's modulus (E) multiplied with second moment of area of cross section (I). Generalized mass is proportional to mass of the beam (m) multiplied by the cube of beam length (l). The α is a proportionality coefficient unique for each mode which depend on the support conditions, but is independent of anatomical differences between bones and animal species. Its value was found to be 3.056 for human Tibia (Van der Perre, 1991). The Pearson's product correlation coefficient (Square of r value) was found as 0.96 between human tibia and bones of 142 different animal species and different types of human bones (Lowet et al., 1992).

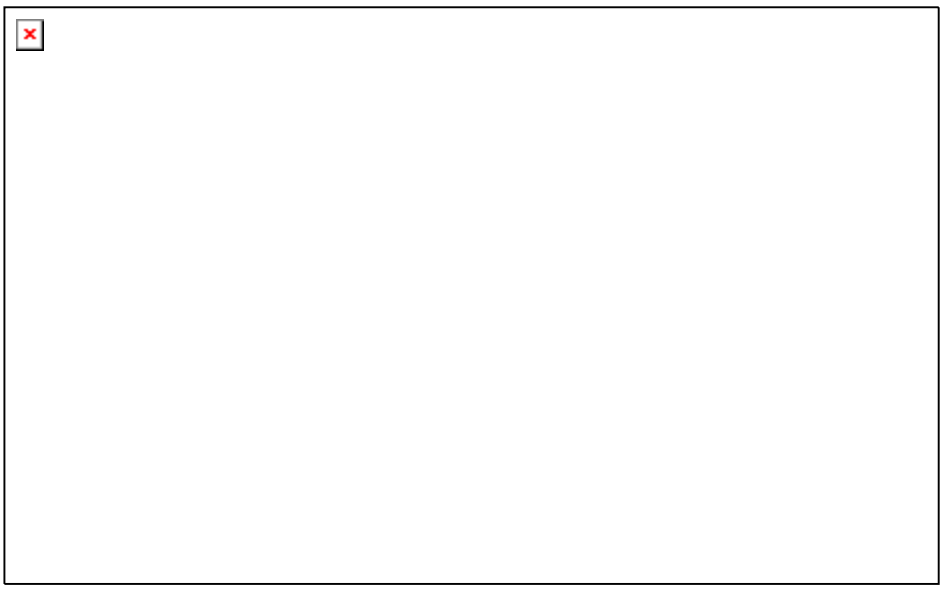

Figure-5.1 (a) Free vibration ; (b) dynamic equilibrium between elastic force and inertial force (Van der Perre, Belgium).

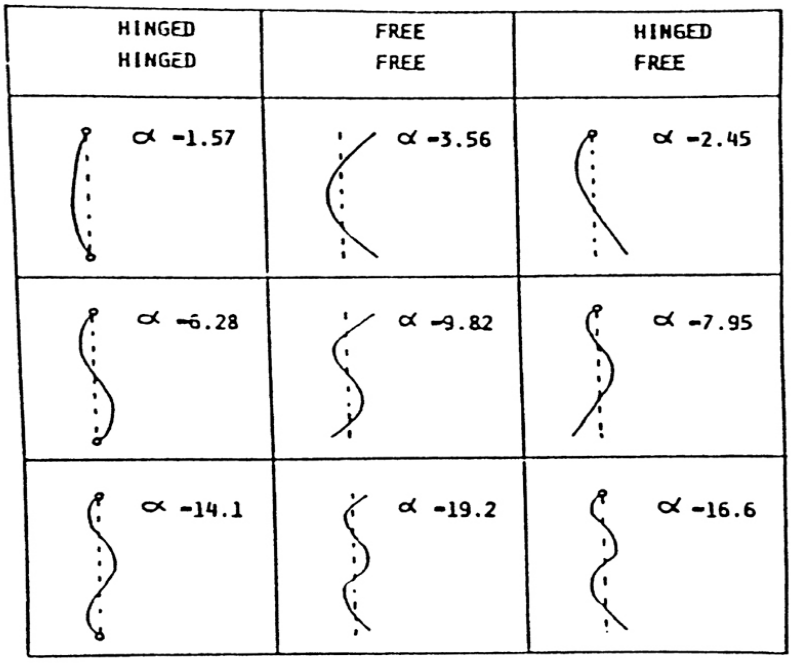

Figure-5.2 Bending modes of a uniform slender beam for three different supporting conditions (Van der Perre, Belgium).

Not only the mode, but also damping has a coefficient which differ in viscous damping where forces resistive to movement are proportional to velocity, and dashpot damping such as in figure above.

As it is understood from the formula 3, modal parameters such as natural frequency, mode shape and damping coefficient, give information about spatial distribution of mass, strength, and damping properties of the structure examined. Two basic types of stimuli can be applied. The first type of stimuli will yield a response related to inputting a number of independent basic frequencies and can be analyzed as such with the aid of the fast Fourier transform, whereas the second type of stimuli is composed of variable frequency cycles of pure sine waves. These are two approaches called impulse response approach and the steady state approach in order to measure natural frequencies. The impulse response method is based on a short force impulse to which the structure responses by a free vibration including structure's free vibration modes. On the other hand, the steady state approach is related to the structures behavior under forced sinodial vibration in the final steady stage. The structure's resistance becomes very low when the forcing frequency

equals one of the natural frequencies of the structure. The frequency response function, hopefully, is made by mini- and micro-computers.

There are several types of modal analysis. One modal analysis can be created by giving a stimulus at one point and measure frequency in a number of representative points. The responses at these points give the ability to determine the mode shapes of the different free vibration modes of a structure. This is the principle of vibration analysis. However, it is also possible to give one excitation and record the response at one point, which is termed as sonic wave propagation analysis where movement of the elements is in the same direction in wave propagation manner. The velocity (c) which is expressed measured propagation time over a known distance depends inversely to the mass density (ρ).

Moreover, it is possible to determine the group velocity that is the velocity at which the whole impulses travel (Sontegard et al., 1976). On the other hand, the wave velocity is frequency-dependent, which means higher frequency components of the signal will be transmitted faster than low frequency components. Based on this characteristic, the term phase velocity has been evaluated which is the velocity at which a single wave of specific frequency can be discriminated from a total wave spectrum (Wong et al., 1983). Based on this method, it is possible to measure the phase velocity of a bending wave from the phase spectra in two points on a tibia in vivo (Stüssi et al., 1988). The frequency response data used in wave phase velocity analysis is the same as in vibration phase difference analysis, but obtained and evaluated with different techniques from a bone with finite dimensions (Collier, 1987.; Stüssi et al., 1988).

Frequencies can also be measured in the case when the bone is considered as a beam of infinite length. The approach is termed as the wave velocity approach when the wave travels in one direction without any reflection at the end without any resonance in contrast to vibration methods. The response of a structure reaches a traveling wave response when the viscous damping increases. The bones are neither free of damping, nor are they damped strong enough to behave ideally. The damping

effect of the surrounding tissue and muscles does not create an ideal model, but this limitation has been corrected by interpretation of frequency response in terms of damped vibration by reconstructed frequency response spectrum or measurements have been taken in a very short time after impulse so that reflected waves have not reached the measurement point (Claessens et al., 1992).

Location of excitation and measurement of resonant frequency have important effects on the results. The radius of gyration measurements performed by application of a force on the medial of lateral surface and posterior surface of radius were based on a incorrect hypothesis in literature (Van der Perre and Cornelissen, 1983). This hypothesis stated that force applied on a free-free body will cause a transverse vibration response and the natural frequency will be determined by the radius of gyration at that direction, too (Collier et al., 1982). However, in contrast to tibia, radius has two single bending modes since it has two mutually axes, x and y, going through the centurion of the cross section.

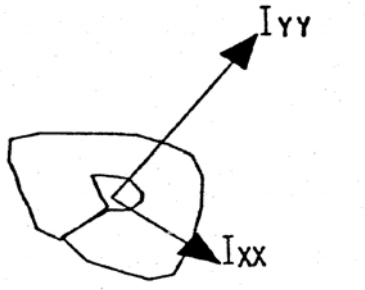

Figure-5.3 Determination of cross-section properties of radius at nearly midshaft (Van der Perre and Cornelissen, 1983).

The natural frequencies fx and fy will be calculated with respect to bending about the x and y axis, respectively. Ixx is the moment of inertia about the x-axis and Iyy is the moment of inertia about the y-axis with only two single bending type modes different to tibia. Therefore, the radius of gyration normal to lateral surface differs from the radius of gyration normal to the medial surface (Van der Perre and Cornelissen, 1983).

Resonant frequency analysis including both vibration analysis and sonic wave propagation has been widely used in clinical applications for monitoring fracture

healing (Cornelissen et al., 1986). It has been found that the natural frequency increased during fracture healing (Borgwardt et al., 1982). The human tibia vibrates free-free in the body since muscles in addition to the effect of soft tissue; joints and fibula provide a viscous damping effect and decrease its frequency (Cornelissen et al., 1986). Mode identification and reproducibility in short term was presented as 5% (Van der Perre et al., 1992) and increased with increasing time. The single bending mode was reproducible enough to be used in clinical area (Cornelissen et al., 1988).

Although several studies have shown that fracture healing can be monitored by vibration analysis (Guzelsu, And Saha, 1981, 1983, 1984; Pelker and Saha, 1983, 1985; Lewis and Goldsmith, 1975; Van der Perre, Belgium), only limited studies have been carried out toward detecting structural changes with aging (Cheng et al., 1995; Selle and Jurist ,1966).

Diagnostic techniques based on measurement of wave propagation characteristics can be helpful in detecting the onset of osteoporotic changes in bones of the entire skeleton. The study concluded that sensile osteoporosis nay have developed in the group aged above 55 based on the phase velocity differing between two groups which were aged above and below 55 years. The difference of phase velocity was also observed between both genders (Chien and Saha, 1987). In this study, resonant frequency analysis was used to determine BMD differences in healthy and osteopenic individuals in terms of natural frequencies. The radius was used because of its superficial location in the body to minimize the soft tissue inferences. The excitation point was chosen as the ending on the styloid process and natural frequency response was recorded at the head of radius.

CHAPTER VI

METHODS AND MATERIALS

6.1 Subjects

Sixty males aged between 50 and 70 year have participated in this study. 30 participants were osteopenic males undergoing medical treatment. Osteopenia was diagnosed in these participants in a population survey and their radial T scores was between -1 and -2.5. Another 30 participants have been randomly selected among healthy individuals. For the randomization of the healthy participants, a physician consulted 75 individuals and determined their health status. Subjects with a history of chronic disease lasting longer than three months that may affect bone metabolism (i.e. renal, hepatic, gastrointestinal, thyroid diseases) were excluded. Other exclusion criteria were history of hormone supplementation (such as corticosteroids), previous low energy fracture, prolonged immobilization (>1 month), over-exposure to irradiation of long-term (over 1 month) and usage of any medication. The participants have been chosen randomly among the remaining ones. Information on the study and possible side effects were given to the participants and a written consent was obtained. Osteopenic participants have been chosen among employees of the institute where the study was performed. All osteopenic participants were under medical treatment for at least two years. Mean age and Body Mass Indexes (BMI) of healthy and osteopenic participants were calculated. Randomization was made in order to obtain experimental and control groups with no significant difference between ages and BMI's of both groups. The age, sex, race, health status

according to BMD, body weight (kg) and height (cm) of the participants were recorded.

6.2 Measurements

6.2.1Dual Energy X-Ray Absorptiometry (DEXA)

One hundred and twenty scans of the dominant and non-dominant forearms of the 60 participants were obtained using the Lunar-DPX® IQ (Madison, Wisconsin, U.S.A) DEXA instrument. The excepted highest radiation dose for each DEXA scan was 0.02 miliRem and the total exposure to radiation of participants at the end of the study was calculated as 0.04 miliRem. Same operator made the scans in order to prevent inter-operator technical errors. Patient positioning was carried out using the instructions and accessories provided by the manufacturer. Analysis was made with the manufacturer's software. The research centre managed routine quality control by ensuring the stability of the DEXA equipment by performing calibrations with machine-specific daily phantom along with monthly phantom measurements provided and controlled by the manufacturer. The mode of measurement was medium.

6.2.2 Quantitative Muscle Strength

An isokinetic dynamometer (Biodex®, Medical System rev. 3,27, New York, USA) was used for the quantitative muscle strength measurements. Peak torque levels and total work achieved in the muscle force-meter was only used for calculations in order to minimize the risk of bias due to differences in motivation to perform the test. The peak torque in flexion and extension were determined at velocities of 60 degrees per second in both the dominant and non-dominant arms. All tests were performed according to the isokinetic protocol advised by the manufacturer in order to ensure the quality and validity of testing. The dynamometer was calibrated prior the study. The body and limbs were secured and the wrist was attached in the horizontal plane at zero degrees. The chair and the dynamometer were

tilted to the zero level as well. The participant moved into position and the dynamometer was placed in front of the wrist of the patient. The axis of rotation of the participant was aligned, stabilized and the ROM (Range of Motion) stops were set. The forearm was stabilized at the 1/3 proximal end of the ulna and radius to prevent interference of upper arms muscular work. Windows'95-based Biodex Advantage Software package was used for the measurements.

Familiarization of the participants with the apparatus before the tests were carried out. Participants performed 5 to 10 repetition of maximal wrist flexion and extension. The concentric mode was chosen and the wrist ROM was limited to 15 degrees of extension and 25 degrees of flexion.

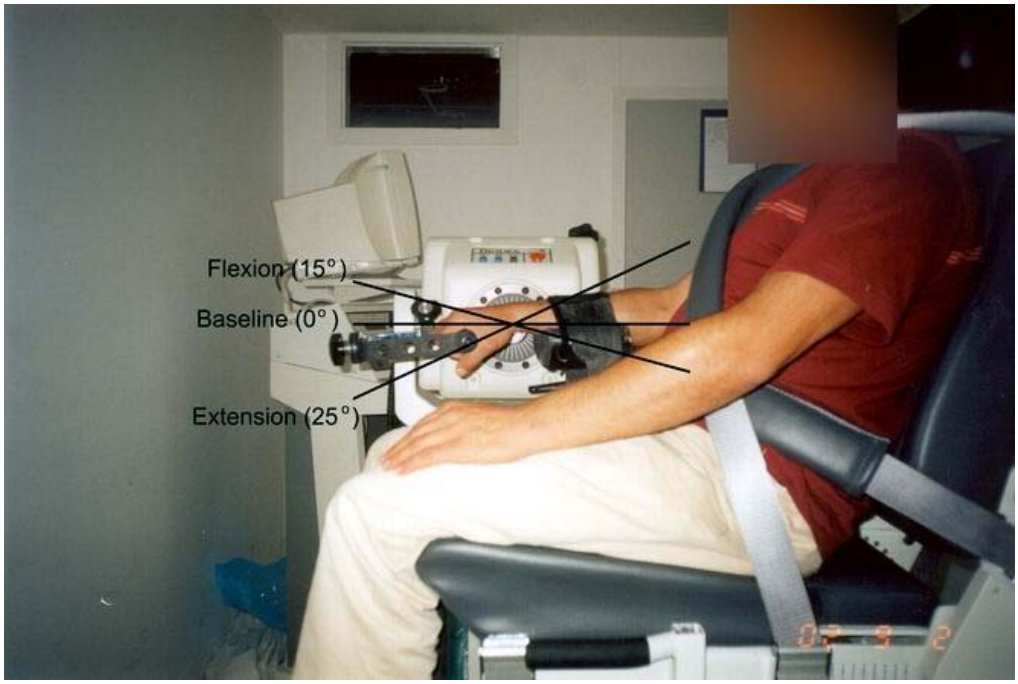

Figure-6.1 Positioning on BİODEX

6.2.3 Vibration Analysis

The vibration analysis was performed via dual channel frequency channel analyzer type 3550 (Bruel and Kjaer, Naerum, Denmark), accelerometer type 4393 with charge sensitivity of 3.16 pC/g, voltage sensitivity of 4.02 mV/g, capacitance of 786 pF and weight 2.2 g; and impact hammer instrumented force transducer type 8202 with sensitivity of 3.49 pC/g and weight of 280g and additional mass of 122g with

4.1 g rubber tip. The excitation point was marked on the anterior surface of radius starting from the head of radius and ending on the styloid process. The location of the excitation points was measured with a caliper. During measurements, the forearm fixation was done at the upper arm and phalengeals to avoid any movement of the arm and thereby preventing incorrect frequency records because of fixation material behaviors. The arm of the subject was placed on a soft matrix to prevent interferences from the table material. The accelerometer was fixed to the soft tissue nearest to the bone with wax. Before each measurement at different arms or subjects, auto range was assessed. The average responses to five excitations were calculated by the software of the instrument and this was repeated two times for each arm to minimize observer errors.

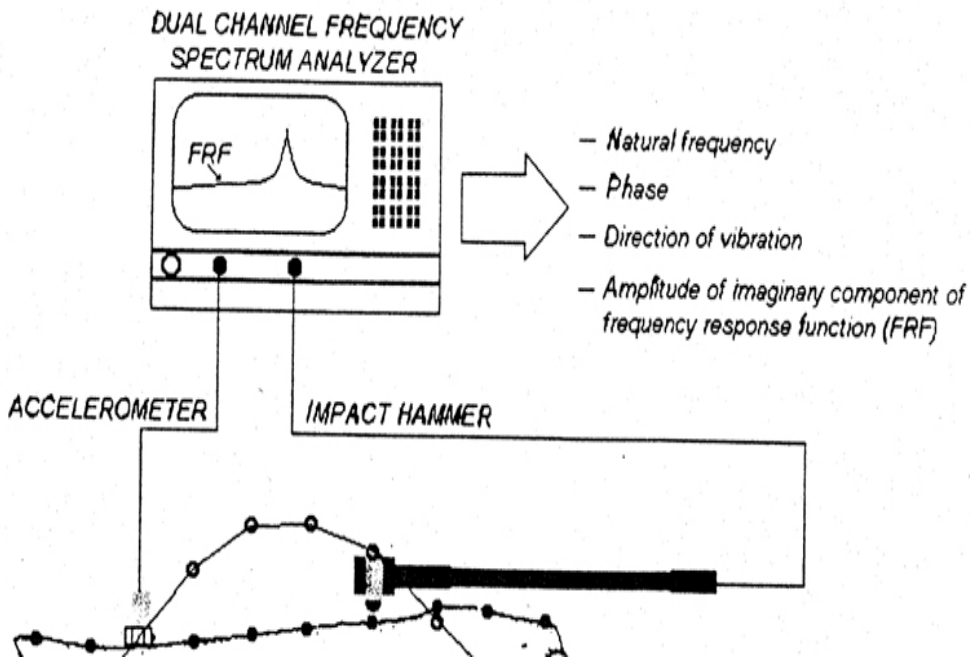

Figure-6.2 Set up for vibration analysis

6.2.4 Quantitative Computed Tomography

Only seven subjects were scanned with the PAL CT Scanner 60/TX (Philips Medical Systems, Koninklijke, Belgium) with an intercept of -520 and scale equal to 0.87 in the CE range of maximum 1600 and minimum -400. During scanning time, lead jacket was worn by subjects in order to prevent excess radiation exposure. Subject positioning was standardized and one qualified radiographer performed all

measurements at the same day. Three cross-sectional scans were made, starting at the distal joint line of the radius. The scan line was positioned using scout view of the scanner after determining the point to be measured with a caliper.

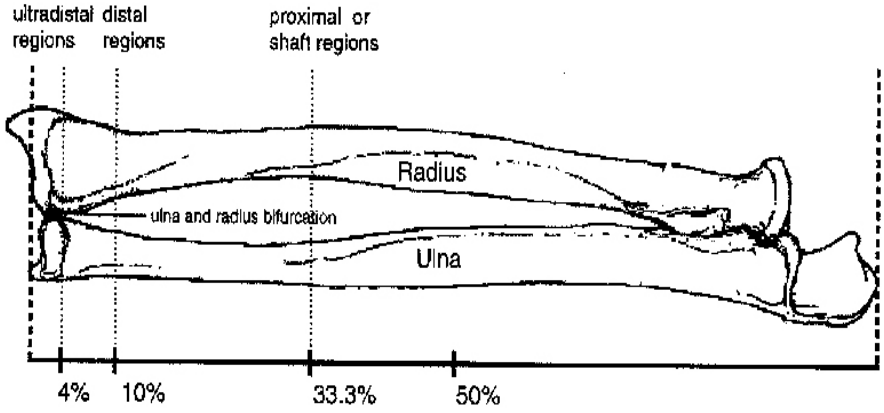

Figure-6.3 Positioning of stimulus and response on the radius

To increase reproducibility, duplicate scans were obtained on another day by the same radiographer. Total slice (scan image) was 7.7 and scan distance was 66mm. Scanogram length was 450 mm with a scanogram tube angle of +90 (vertical). Tube voltage was adjusted to 100 and 130 kV with a tube current of 250 mA. The field of view was H250 with a scanning time of 3.05 seconds and +0 granular angulations. The convolution filter was adjusted to 4C and matrix size of 10 mm thick sizes was 512. The average bone, trabecular bone, and cortical bone CT numbers were separately calculated. The density for each pixel in the related components of the bone in healthy and osteopenic individuals was obtained by utilizing equation where matrixes were selected as 4X4 and 2X6 to optimize and standardize the calculations. Parameters related to geometry were determined by QCT. These were;

- the width of radius in x axis in both arms (Figure-6.4)
- the width of radius in y axis in both arms (Figure-6.5)
- the width of trabeculae in radius in x axis in both arms (Figure-6.6)
- the width of trabeculae in radius in y axis in both arms (Figure-6.7)
- the cortical thickness of radius in both arms (Figure-6.8)

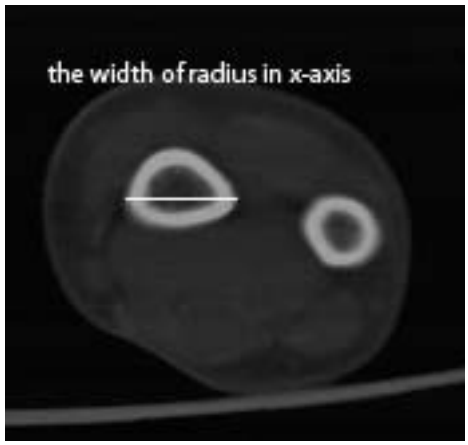

Figure-6.4 the width of radius in x-axis in non-dominant arm

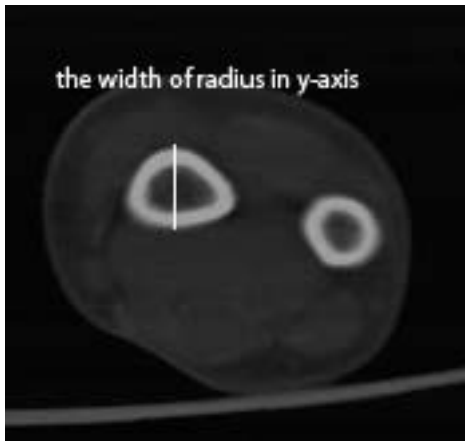

Figure-6.5 the width of radius in y-axis in non-dominant arm

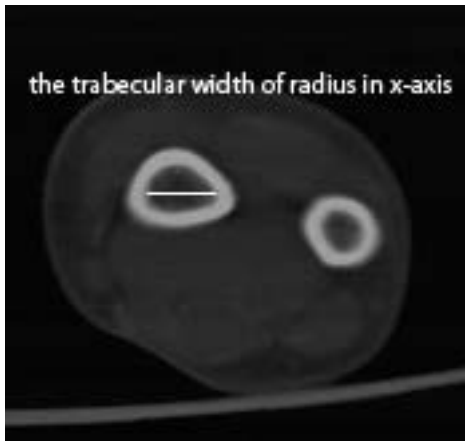

Figure-6.6 the trabecular width in x-axis in non-dominant arm

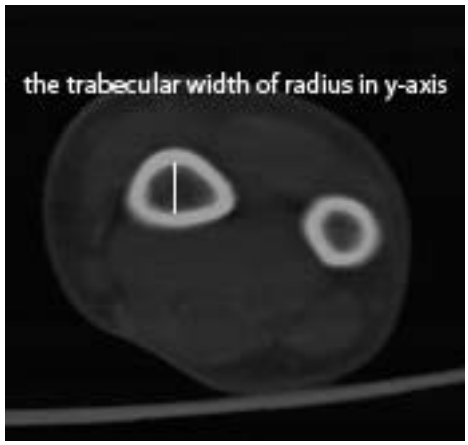

Figure-6.7 the trabecular width in y-axis in non-dominant arm

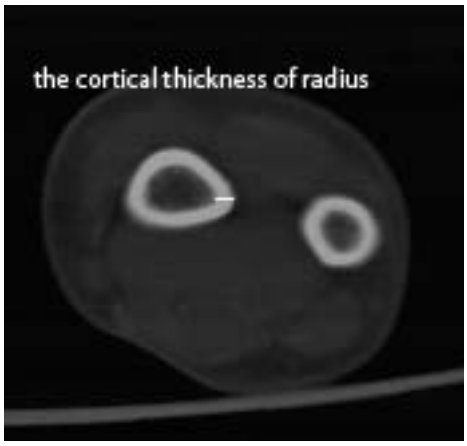

Figure-6.8 Cortical thickness in radius in non-dominant arm

6.3 Statistical Analysis

Means and standard deviations of BMD, natural frequency and muscle strength in healthy and osteopenic group were calculated and compared with One-way ANOVA (two tailed ; $\alpha = .005$) using SPSS 10.0 for Windows statistic software package. The Pearson Product Moment Correlation Coefficient was conducted to determine correlations between these parameters either in healthy and osteopenic groups, or according to dominancy. Pearson's product correlation coefficient was used to determine the relationship of triple images obtained from radius. Moreover, QCT measurement results were analyzed with Pearson's product correlation coefficient analysis in order to state the correlation between BMD measured as total, trabecular and cortical, NF and bone geometry stated as lengths in x and y directions,

trabecular width in x and y, and cortical thickness in radius in both dominant and non-dominant arms of seven subjects including healthy and osteopenic individuals.

CHAPTER VII

RESULTS

7.1 Desciptive statistic of 60 individuals results based on health status

There was no significant difference between groups according to age, weight, height and body mass ındex (BMI).

Table-1 Statistics of measurements obtained by 60 subjects

GROUPS	Age (years)	Std	Weight (kg)	Std	Heigth (cm)	Std	BMI (kg/m^2)	Std
Healthy	59.7	6.6	70.0	8.1	173	4.4	26.6	8.1
Osteopenic	57.8	4.2	64.5	1.5	169.3	4.1	25.2	01.1

Table-2 Means and standard deviations of measured parameters

	HEALTHY GROUP				OSTEOPENIC GROUP			
	Dominant arm		Nondominant arm		Dominant arm		Nondominant arm	
	Mean	Std	Mean	Std	Mean	Std	Mean	Std
Bone mineral density (BMD)	,45[a]	,05	,44[b]	,05	,37[a]	,04	,36[b]	,04
Peak Torque in Extension (PTE)	13,27[a]	2,80	12,26[b]	2,48	10,89[a]	3,72	10,75[b]	2,86
Peak Torque in Flexion (PTF)	18,38[a]	6,66	15,89	5,91	14,40[a]	6,55	15,89	5,91
Total Work in Extension (TWE)	31,57[a]	6,06	30,04	6,31	26,30[a]	9,10	26,69	8,11
Total Work in Flexion (TWF)	41,21[a]	17,42	32,70	15,66	32,11[a]	17,62	24,85	16,22
Natural Frequency (NF)	88,20[a]	15,88	80,70[b]	7,56	70,90[a]	18,94	65,73[b]	16,68

Similar letters show statistically significant difference at .05

The means and standard deviations of DEXA, BIODEX and Vibration Analysis results of healthy and osteoporotic groups were calculated (Table 1).

One-way ANOVA (two tailed; $\alpha = .05$) was performed to state the difference between means within and among groups according to health and dominancy Box plot representation of all parameters according to health status were drawn.

There was a significant difference in BMD values measured in the dominant ($F = 42{,}03$; $p < .001$) (Figure-7.1) and non-dominant ($F = 37{,}04$; $p < .001$) (Figure-7.2) arms between healthy and osteopenic participants.

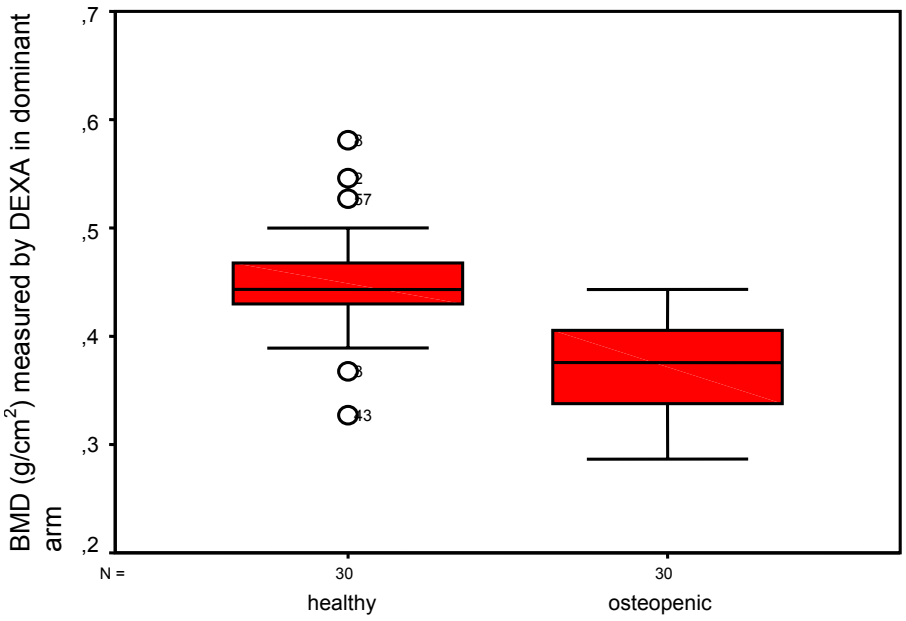

Figure-7.1 Radial BMD of the dominant forearm measured by DEXA

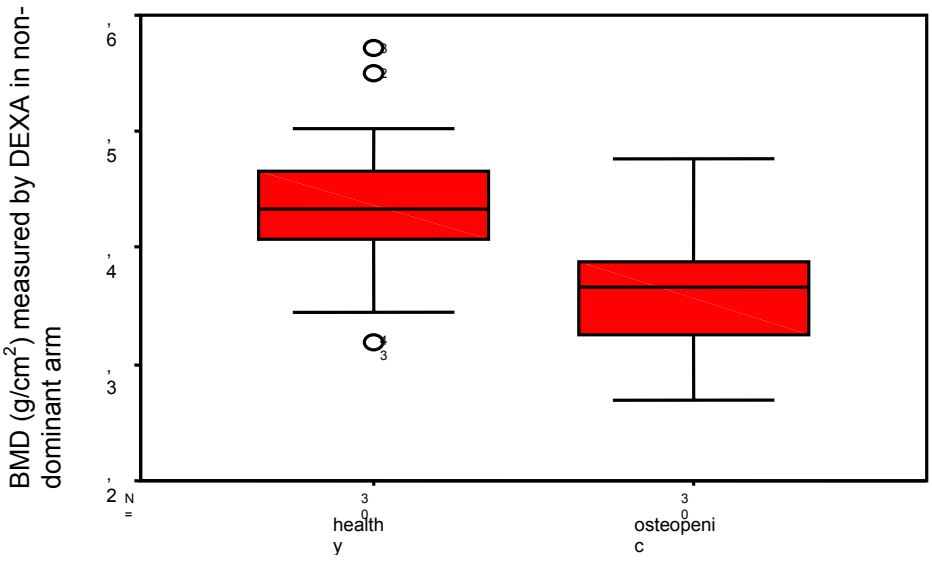

Figure-7.2 Radial BMD of the non-dominant forearm measured by DEXA

There was also a significant difference in peak torque in extension of the dominant (F = 7,80; p = .007) (Figure-7.3) and the non-dominant arms (F = 4,79; p = .03) (Figure-7.4) between healthy and osteopenic groups.

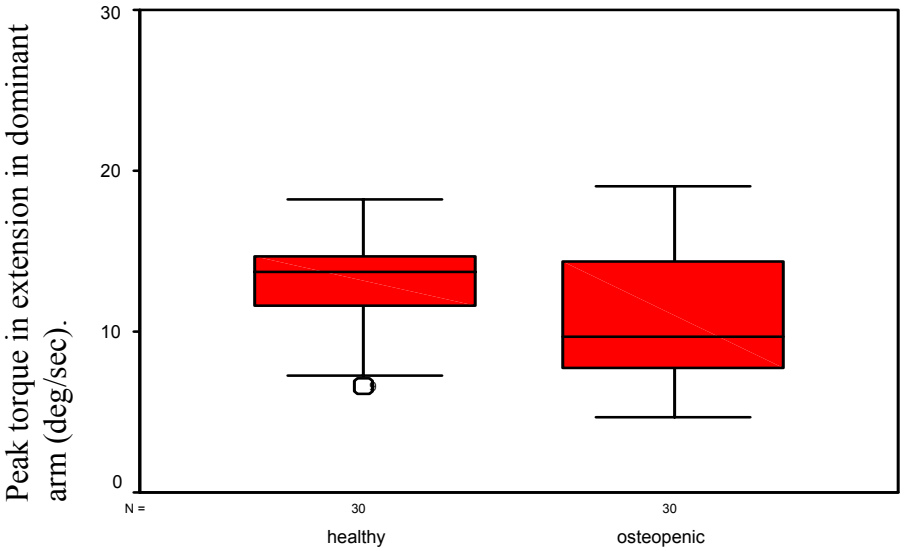

Figure-7.3 BIODEX value of Peak Torque in Extension of dominant arm measured at 60^0/sec

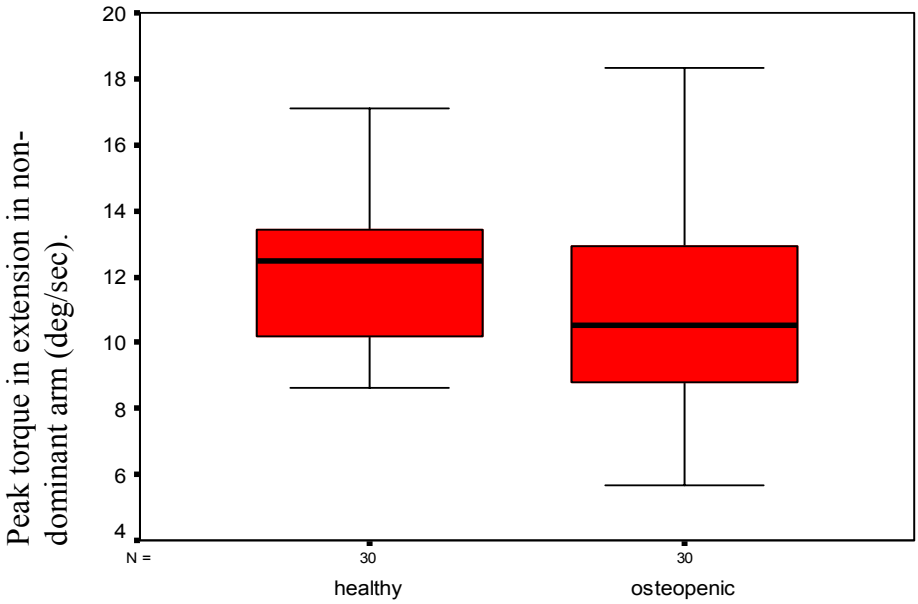

Figure-7.4 BIODEX value of Peak Torque Extension of non-dominant arm measured at 60^0/sec

A significant difference was found between osteopenic and healthy participants in peak torque in flexion measured on the dominant arm (F = 5,44 ; p = ,023) (Figure-7.5), but significant difference was not observed in the non-dominant arm (Figure-7.6).

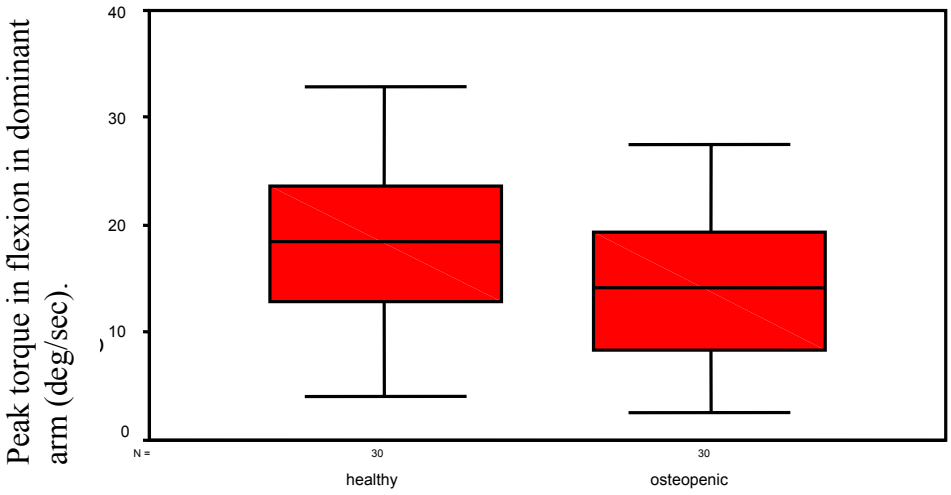

Figure-7.5 BIODEX value of Peak Torque in Flexion of dominant arm measured at 60^0/sec

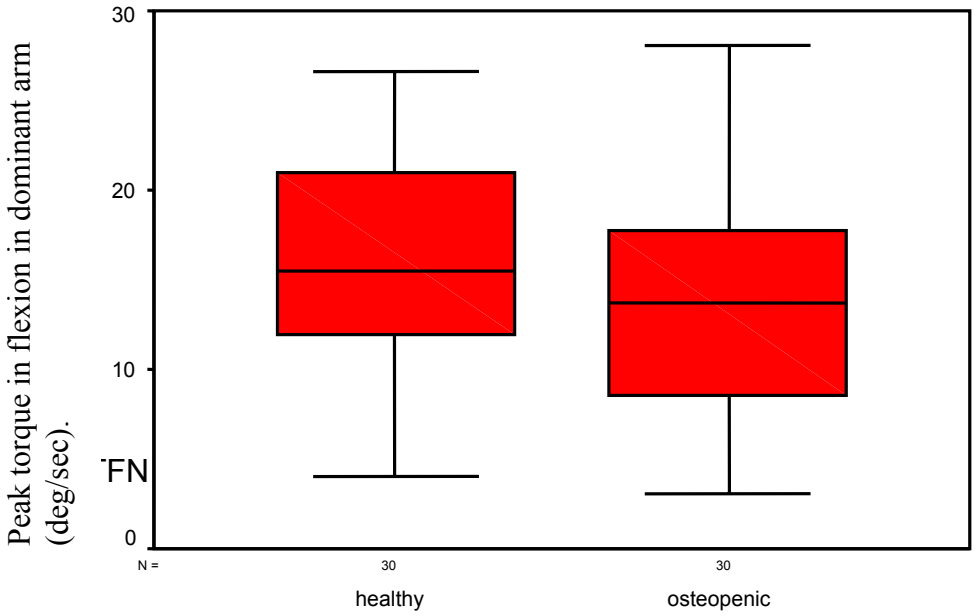

Figure-7.6 BIODEX value of Peak Torque in Flexion of dominant arm measured at 60^0/sec.

The difference between healthy and osteopenic participants was significant in total work in extension (F = 6,98¸p = ,01) (Figure-7.7) and flexion (F = 4,05; p = 0,049) (Figure-7.8) in the dominant arm, but does not show any significance in the non-dominant arm (Figure-7.9 and 7.10).

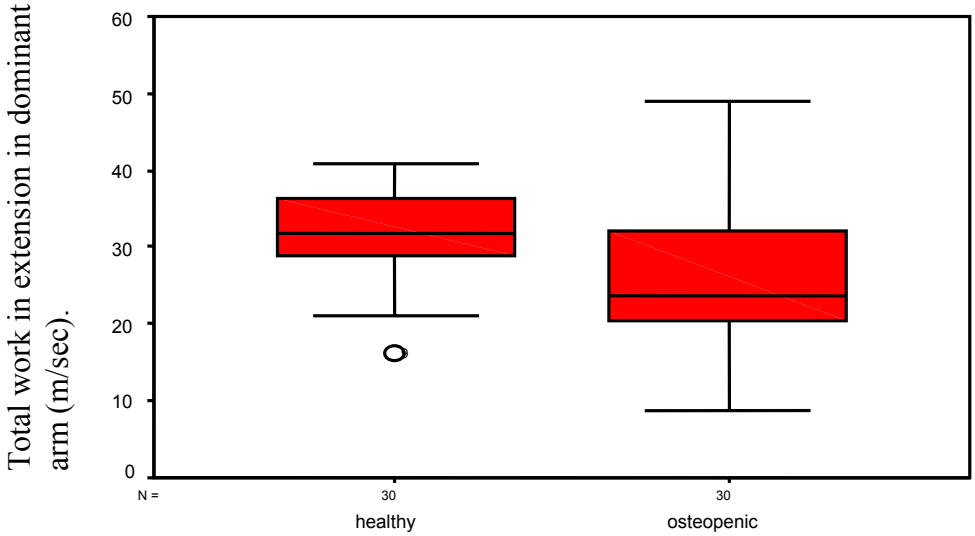

Figure-7.7 BIODEX value of total work in extension in dominant arm at 60 m/sec

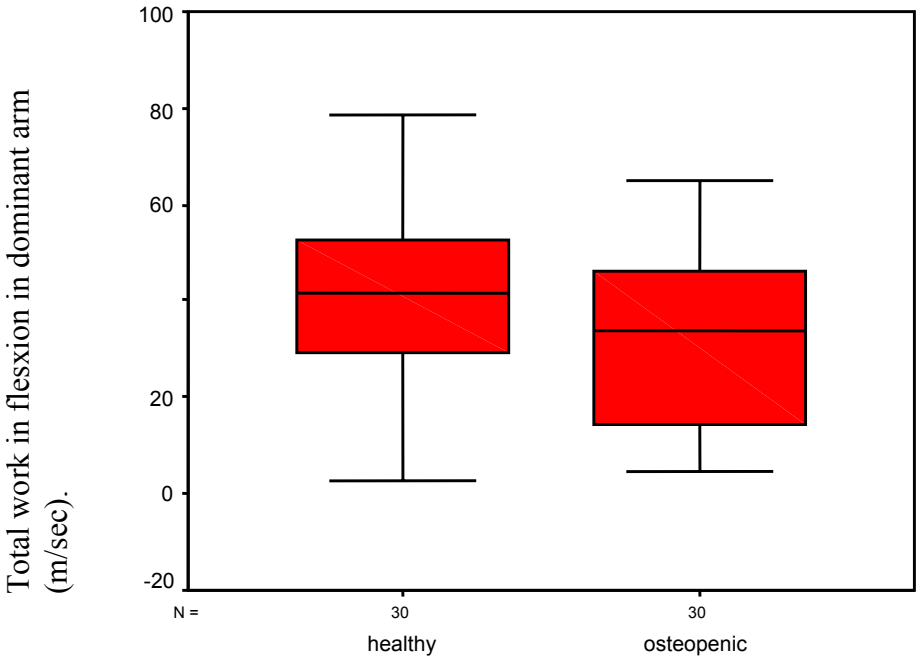

Figure-7.8 BIODEX value of Total work in Flexion in non-dominant arm at 60 m/sec

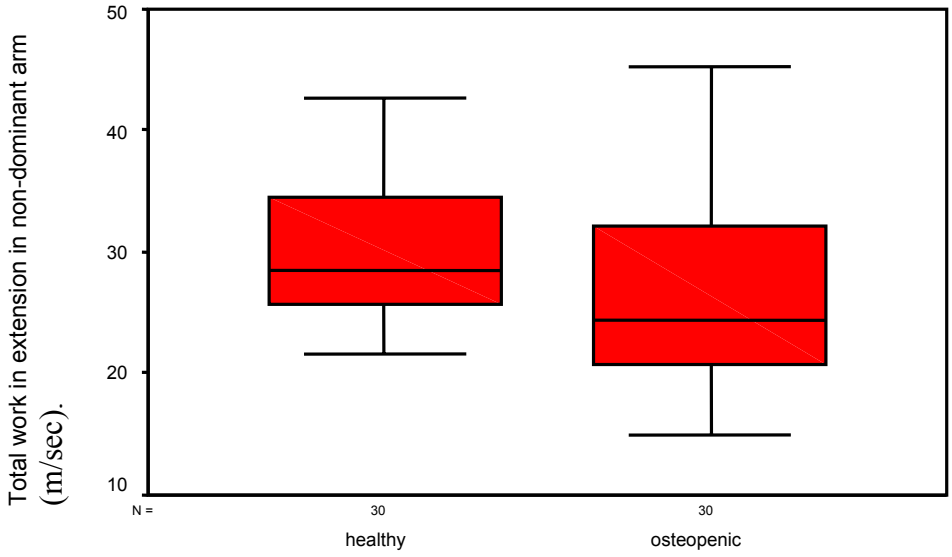

Figure-7.9 BIODEX value of total work in extension in non-dominant arm at 60 m/sec

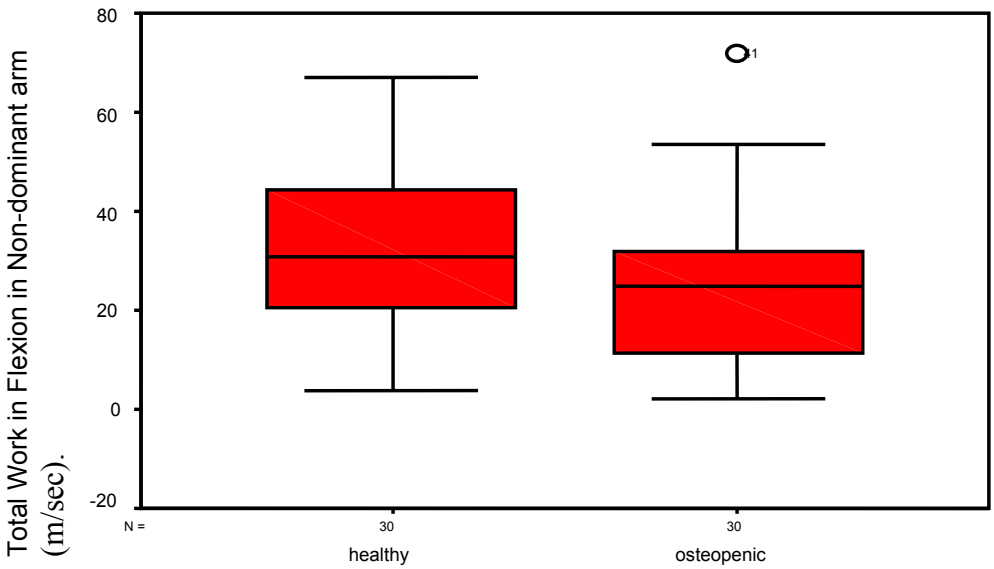

Figure-7.10 BIODEX value of total work in flexion in non-dominant arm at 60 m/sec

Moreover, the difference in natural frequency between healthy and osteopenic participants was significantly in both dominant ($F = 18,04$; $p < .001$) (Figure-7.11) and non-dominant arms ($F = 19,99$; $p = .01$) (Figure-7.12).

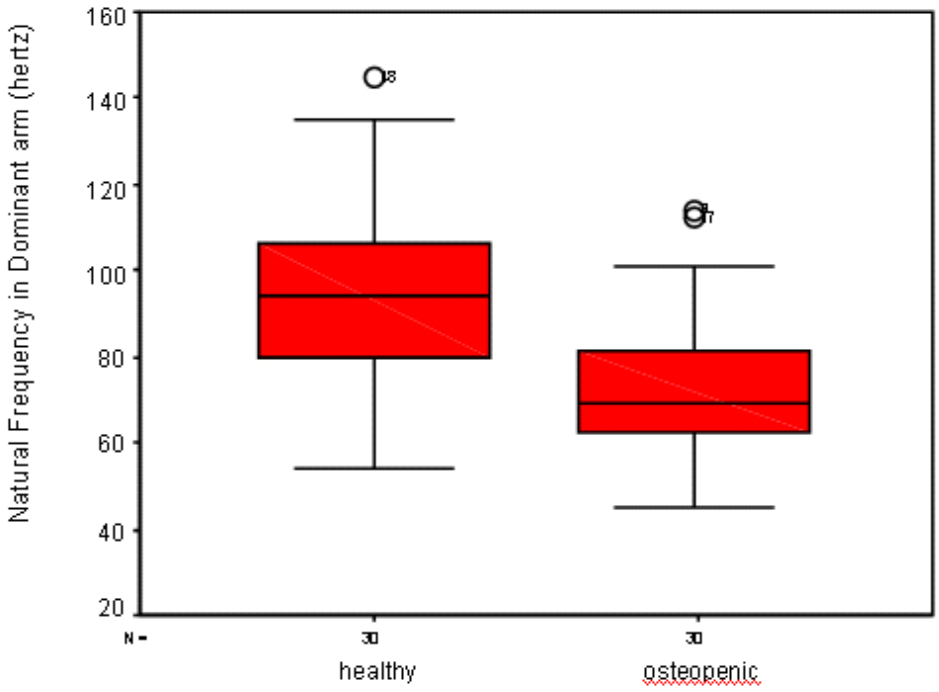

Figure-7.11 Natural frequency in dominant arm in healthy and osteopenic group

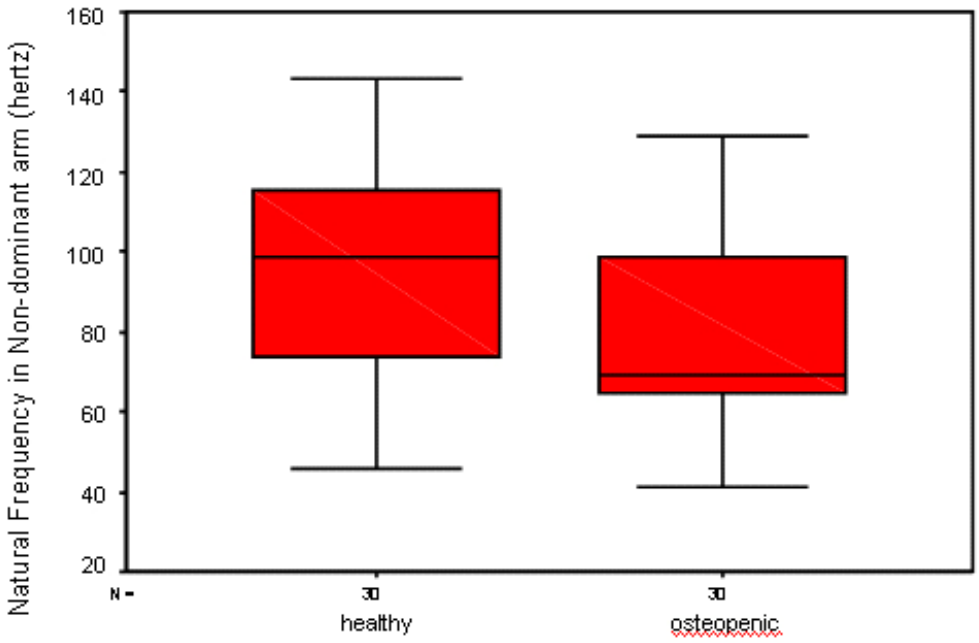

Figure-7.12 Natural frequency in dominant arm in healthy and osteopenic group

7.2 Correlations between BMD, NF and muscle strength parameters in dominant and non-dominant arms

Means and standard deviations of BMD, PTE, PTF, TWE, TWF, and NF in the combined groups were calculated in dominant (Table 3), and non-dominant arms (Table 4).

Table-3 Descriptive Statistics of the dominant arm (n = 60)

	Mean	Std
Bone mineral density (g/cm^2)	0,411	0,06
Peak torque in extension (deg/sec)	12,07	3,48
Peak torque in flexion (deg/sec)	16,39	6,85
Total work in extension (m/sec)	28,93	8,11
Total work in flexion (m/sec)	36,66	17,97
Natural frequency (hertz)	70,90	19,84

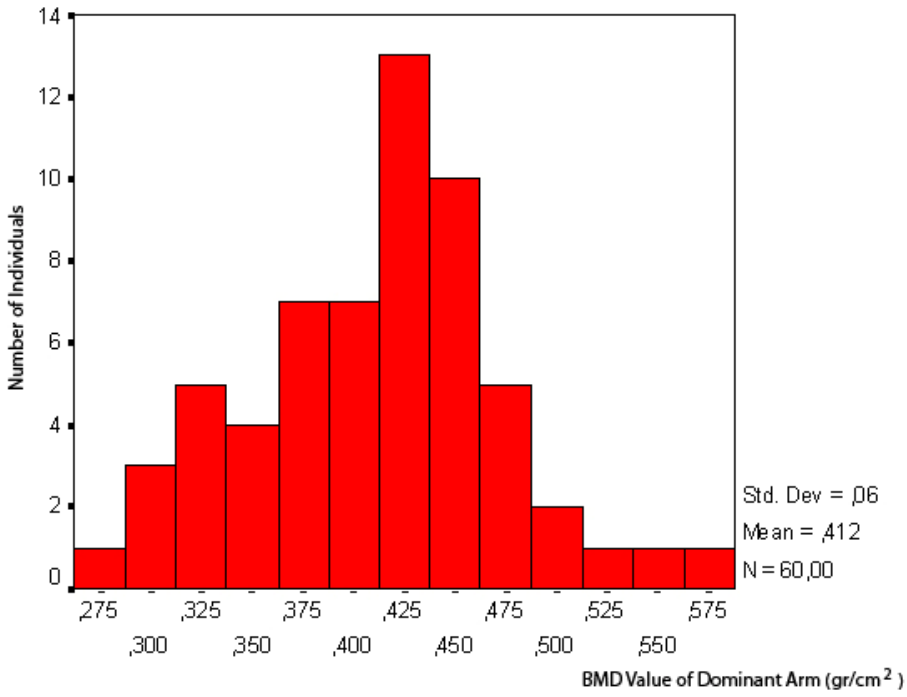

Figure-7.13 Dispersion of BMD value in dominant arm of all participants

Table-4 Descriptive Statistics of the non-dominant arm (n = 60)

	Mean	Std
Bone mineral density (g/cm^2)	0,40	0,06
Peak torque in extension (deg/sec)	11,50	2,76
Peak torque in flexion (deg/sec)	14,64	6,15
Total work in extension (m/sec)	28,36	7,40
Total work in flexion (m/sec)	28,77	16,30
Natural frequency (hertz)	65,73	16,67

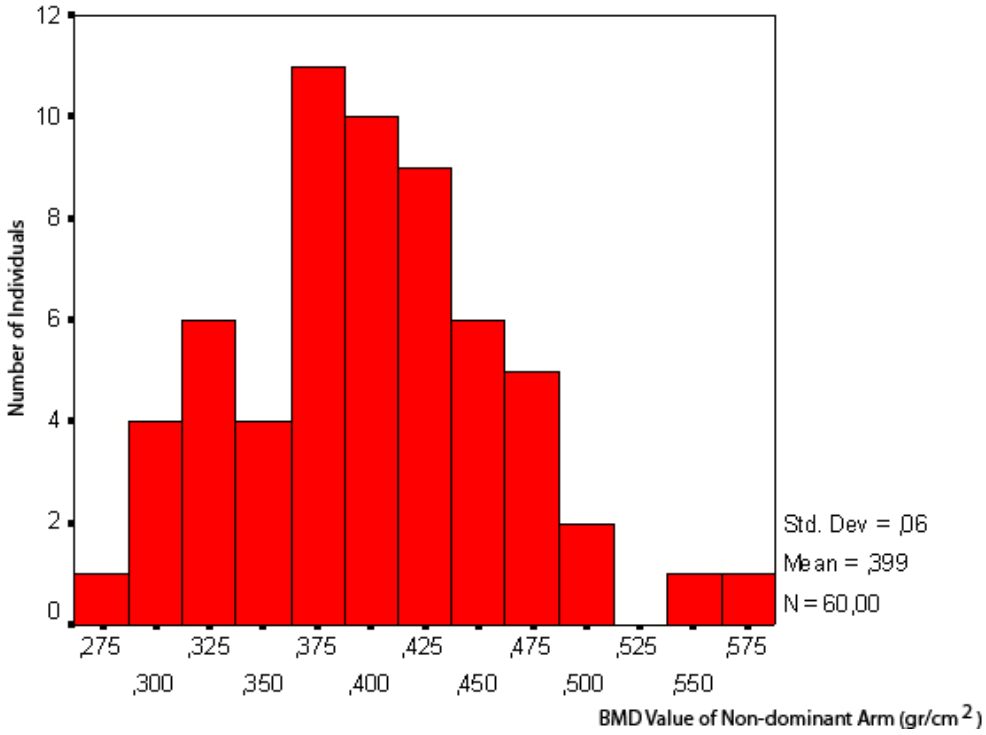

Figure-7.14 Dispersion of BMD value in non-dominant arm of all participants

There was a moderate positive correlation (r = ,59 ; p < ,001) between BMD and natural frequency, and a low to moderate positive correlation between BMD and muscle strength expressed as peak torque in extension (r = ,36; p = ,005), peak torque in flexion (r = ,31; p = ,016), total work in extension (r = ,28; p = ,030) and total work in flexion (r = ,27; p = ,041) in the dominant arms of 60 subjects (Table 4). Moreover, there was a significantly positive correlation moderate in magnitude between BMD and natural frequency (r = ,643; p<,001) in the non-dominant arms of

60 individuals. The correlation between muscle strength and BMD was not significant in the non-dominant arm.

Table-5. Correlation coefficient values for dominant arm

	PTE	PTF	TWE	TWF	NF	
BMD	,36**	,31*	,28*	,27*	,59**	r value
	,005	,016	,030	,041	,001	p value

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

7.3 Results of different scan sites of QCT in the same arms

The bone mineral density of radius was calculated as trabecular BMD, cortical BMD and total BMD in dominant and non-dominant arms of healthy and osteopenic groups. The correlation of BMD between slice 1,2 and 3 in the radius according to trabecular, cortical or total BMD was not statistically significant in the right arm. Moreover, there was no significant correlation in radius trabecular BMD between slice 1, 2 and 3, however, there was a significantly strong positive correlation between slice 1 and 2 in total BMD ($r= ,85$; $p < ,001$) and cortical BMD ($r= ,96$; $p < ,001$) of the radius in the non-dominant arm.

7.4 Results of QCT based on bone geometry

A statistically significant positive correlation ($r = ,81$; $p = ,039$) was observed between average BMD measured by QCT and by DEXA. Moreover, there was a significant positive correlation between radial average BMD and radial width ($r = ,82$; $p = ,03$) and radial trabecular width ($r = ,76$; $p = ,05$). Moreover, radial average BMD was also strongly positive correlated to radial cortical thickness ($r = ,89$; $p = ,007$) and natural frequency ($r = , ,89$; $p = ,008$).

There was no significant correlation between slices in terms of trabecular BMD in the non-dominant arm. On the other hand, there was a strong positive

correlation between the slice 1 and 2 in the average BMD (r = ,85; p = ,03) and cortical BMD (r = ,96; p = ,001). Cortical BMD was significantly correlated to both average BMD in slice 1 (r = ,94; p = ,006) and average BMD in slice 2 (r = ,86; p = ,027). Moreover cortical thickness showed statistically strong positive correlation to both BMD obtained by DEXA (r = ,81; p = ,026) and natural frequency (r = ,82; p = ,024) in the non-dominant arm. There was also a strong positive correlation between BMD measured by DEXA and natural frequency (r = 86; p = ,014), whereas size of the bone expressed as trabecular width, radial width in x and/or y direction does not show any significant correlation to either average BMD measured by DEXA and QCT, and natural frequency.

Table-6 Correlation coefficient values between natural frequency and bone parameters in dominant arm

Natural Frequency	Cortical thickness	,81**
	Radial average BMD by QCT	,89**
Radial average BMD	Radial width in x axis	, 82*
	Radial trabecular width	,76*

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Table-7 Correlation coefficient values between natural frequency and bone parameters in non-dominant arm

Natural Frequency	Cortical thickness	,82*
Cortical BMD in $slice_1$	Cortical thickness in $slice_1$	,96**
	Radial average BMD in $slice_1$	, 94**
	Radial average BMD in $slice_2$	,86 **

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

CHAPTER VIII

DISCUSSION

8.1 Differences and correlations between BMD, natural frequency and muscle strength in dominant and non-dominant arms of both groups

One of the purposes of this study was to determine the differences between BMD, natural frequency and muscle strength in healthy and osteopenic participants in both dominant and non-dominant arms. A statistically significant difference between osteopenic and healthy participants was presented not only in BMD, but also in natural frequency in both arms. The difference in natural frequencies in dominant and non-dominant arms was parallel to the difference in BMD in both groups. This shows that there may be a correlation between BMD and natural frequency in the bone. These difference in BMD between healthy and an osteopenic group shows that radius can be used to estimate BMD at remote anatomical locations and thereby estimate risk of fractures. Moreover, peripheral location of the radius results in reduced radiation dose to the gonads and made this site an early choice for the detection of osteoporosis (Augat et al., 1998).

The difference between groups according to muscle strength was statistically significant in the dominant arm, however, did not differ between healthy and osteopenic participants in the non-dominant arm. This difference can be explained by the usage frequency of these arms in our daily life (Vuori et al., 1994). The magnitude of difference, being greater in flexion may be explained with three

muscles in the forearm responsible in the flexion and suppination, whereas only one muscle performs extension in a more limited range of motion. In other words, flexion is performed by the agonist action of biceps branchii, branchioradialis that insert in radius and branchialis that insert in the coronoid process of ulna (Seeley, Stephens and Tate, 1999). This results in a more resistant state since the effect of these muscles is coupled gradually. The more a muscle is used, the higher will be its strength. Muscle strength increases with increasing load exposed progressively and continuously; that is also an accepted principle in training (Alfredson et al., 1998).

Muscles are more sensitive than bones in response to load. Changes in BMD occur only when a certain threshold in loading is reached and in a slower rate compared to muscles. Thus, in order to stimulate bone metabolism positively, skeletal load has to be increased over long periods and above the threshold values of the modeling metabolism (Düppe et al., 1997; Frost, 2001). High impact activities such as squash, tennis and badminton are more osteogenic than running, cycling or swimming (Karlsson et al., 1993). Weight lifters presented greater BMD in their forearms that might be related to weight bearing exercises (Karlson et al., 1993). Since the participants were sedentary individuals, the skeletal loading was limited to daily activities, still presenting a positive correlation between muscle strength and BMD, but low to moderate.

Another purpose of this study was to determine the correlation between BMD, natural frequency and muscle strength in healthy and osteopenic participants in both dominant and non-dominant arms. A statistically significant positive correlation moderate in magnitude was observed between forearm BMD and natural frequency in both arms of healthy and osteopenic individuals. The correlation in the non-dominant arm was slightly higher when compared with the dominant hand in both groups. This may be a result of different musculature in both arms. The effect of soft tissue, joints and fibula provide a viscous damping effect and decrease its frequency (Cornelissen et al., 1986).

The behavior of musculature and soft tissue enveloping ulna was studied previously and the muscles were modeled as a indefinite series of uniformly distributed, parallel, spring-mass-damper system attached to the ulna. By constructing an impedance curve, it was concluded that some sort of sub-resonance occur associated with musculature attached to ulna (Orne and Mandke, 1975; Thompson et al., 1976). This effect was not observed in the study with tibia where bones were enveloped by groups of bigger musculature (Cornelissen et al., 1986).

The peripheral location of the forearm in addition to negligible soft tissue correction improves the accuracy and precision of BMD measurements by vibration analysis. Mode identification and reproducibility in short term was presented as 5% (Van der Perre et al., 1992) and increased with increasing time.

Only the single bending mode was determined in a nearly free-free model in radius. The natural frequency measured in terms of he single bending mode was reproducible enough to be used in clinical area (Cornelissen et al., 1988).

8.2 Correlation between BMD, geometrical properties of the bone and natural frequency

The positive correlation between natural frequency and BMD measured by DEXA does not have the same magnitude with the correlation obtained from total radial BMDs measured by QCT. Moreover, average BMD is highly affected by the width of the bone and to lesser extends by the trabecular width. DEXA measures an average BMD of the radius which is identical to the total radial BMD measured with QCT. On the other hand, natural frequency was strongly correlated to the cortical thickness that has a higher density than trabecular bone and effect also the average BMD in the bones. Moreover, disuse osteoporoses related to aging and reduce in physical activity results in cortical thinning rather than affecting the trabecular component of the bone (Burstein et al., 1969). A study concluded that sensile osteoporosis may have developed in the group aged above 55 based on the phase velocity differing between two groups which were aged above and below 55 years.

The difference of phase velocity was also observed between both genders (Chien and Saha, 1987).

In this study, resonant frequency analysis was used to determine BMD differences in healthy and osteopenic participants in terms of natural frequencies. The radius was used because of its superficial location in the body to minimize the soft tissue inferences. The excitation point was chosen as the ending on the styloid process and natural frequency response was recorded at the head of radius.The results represents that vibration analysis measurement technique may as reliable as DEXA in monitoring BMD loss in distal radius.

Moreover, there was also a strong positive correlation between cortical thickness and natural frequency which can be explained with the continuous structure of the cortical side when compared to the network structure of the trabecular. The stronger magnitude in correlation between natural frequency and cortical thickness compared to total BMD can be a result of the higher density in the cortical region of the bone compared to the average BMD bone and is closer related to bone strength than bone mineral density.

The accuracy of acceleration measurements strongly depends on the method of accelometer attachment; Bone Mounted accelerometer (BMA) or skin mounted accelerometer (SMA). While BMA is the better indication of bone acceleration, it is clearly not a practical method for in vivo assessment. SMA, while being easy to accomplish, suffers generally from low stiffness of attachment and leads to low measurement system bandwidth (Wosk and Voloshin, 1981; Light et al., 1980). Many studies have tried to overcome this problem by preloading the skin layer between an SAM and the underlying bone (Saha, 1987; Collier, 1987). The results obtained from Lewis and Ziegert's studies showed that the weight of the accelerometer was a critical point in overcoming this limitation. A 34 gram skin surface accelerometer gave outputs with little resemblance to the bone motions, appearing to oscillate at its NF of the soft tissue. A 1.5 gram skin surface accelerometer showed nearly identical outputs to the bone accelerations (Ziegert and Lewis, 1979). The results obtained with accelerometer type 4393 with charge

sensitivity of 3.16 pC/g, voltage sensitivity of 4.02 mV/g, capacitance of 786 pF and weight 2.2 g was found to be enough to give reasonable results in the radius by vibration analysis.

The damping value may range from 10% to 16% with the best results obtained by free-free mode. The damping mode was nearly free-free in this study by excitation and recording the radius before the waves reach the articulations on both ends. Location of excitation and measurement of resonant frequency have important effects on the results. The response of a structure reaches a traveling wave response when the viscous damping increases. The bones are neither free of damping, nor are they damped strong enough to behave ideally. The damping effect of the surrounding tissue and muscles does not create an ideal model, but this limitation has been corrected by interpretation of frequency response in terms of damped vibration by reconstructed frequency response spectrum or measurements have been taken in a very short time after impulse so that reflected waves have not reached the measurement point (Claessens et al, 1992).

The radius of gyration measurements performed by application of a force on the medial of lateral surface and posterior surface of radius were based on a incorrect hypothesis in literature (Van der Perre and Cornelissen, 1983). This hypothesis stated that force applied on a free-free body will cause a transverse vibration response and the natural frequency will be determined by the radius of gyration at that direction, too (Collier et al., 1982). However, in contrast to tibia, radius has two single bending modes since it has two mutually axes, x and y, going through the centurion of the cross section. Location of excitation and measurement of resonant frequency have important effects on the results. The radius of gyration measurements performed by application of a force on the medial of lateral surface and posterior surface of radius were based on a incorrect hypothesis in literature (Van der Perre and Cornelissen, 1983). This hypothesis stated that force applied on a free-free body will cause a transverse vibration response and the natural frequency will be determined by the radius of gyration at that direction, too (Collier et al., 1982).

8.3 Conclusion

Previous studies stated that the use of natural frequencies alone appears to be of limited value in diagnosis of osteoporosis as a result of decrease in BMD (Doherty; 1971, 1974; Markey and Jurist, 1974, Lewis, 1975, Lewis and Tarr;1975). On the other hand, Jurist (1970) obtained correlations between ulnar natural frequencies and the degree of osteoporosis. According to these results of the study, it can be concluded that vibration analysis is a precise method in predicting the bone strength which depends highly on its size, shape and the distribution of its trabecular and cortical components. The difference in the magnitude of correlation between natural frequency and bone mineral density measured by DEXA and QCT stated that average BMD does not provide enough precise information about bone strength and type of bone mineral loss. Moreover, differences in correlation between natural frequency and trabecular width and cortical thickness showed that geometry and the ratio of these components have an effect on both natural frequency and BMD where natural frequency is mostly affected by cortical thickness. The moderate positive correlation between BMD and muscle strength in sedentary participants showed that exercise may have an effect on bone remodeling.

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